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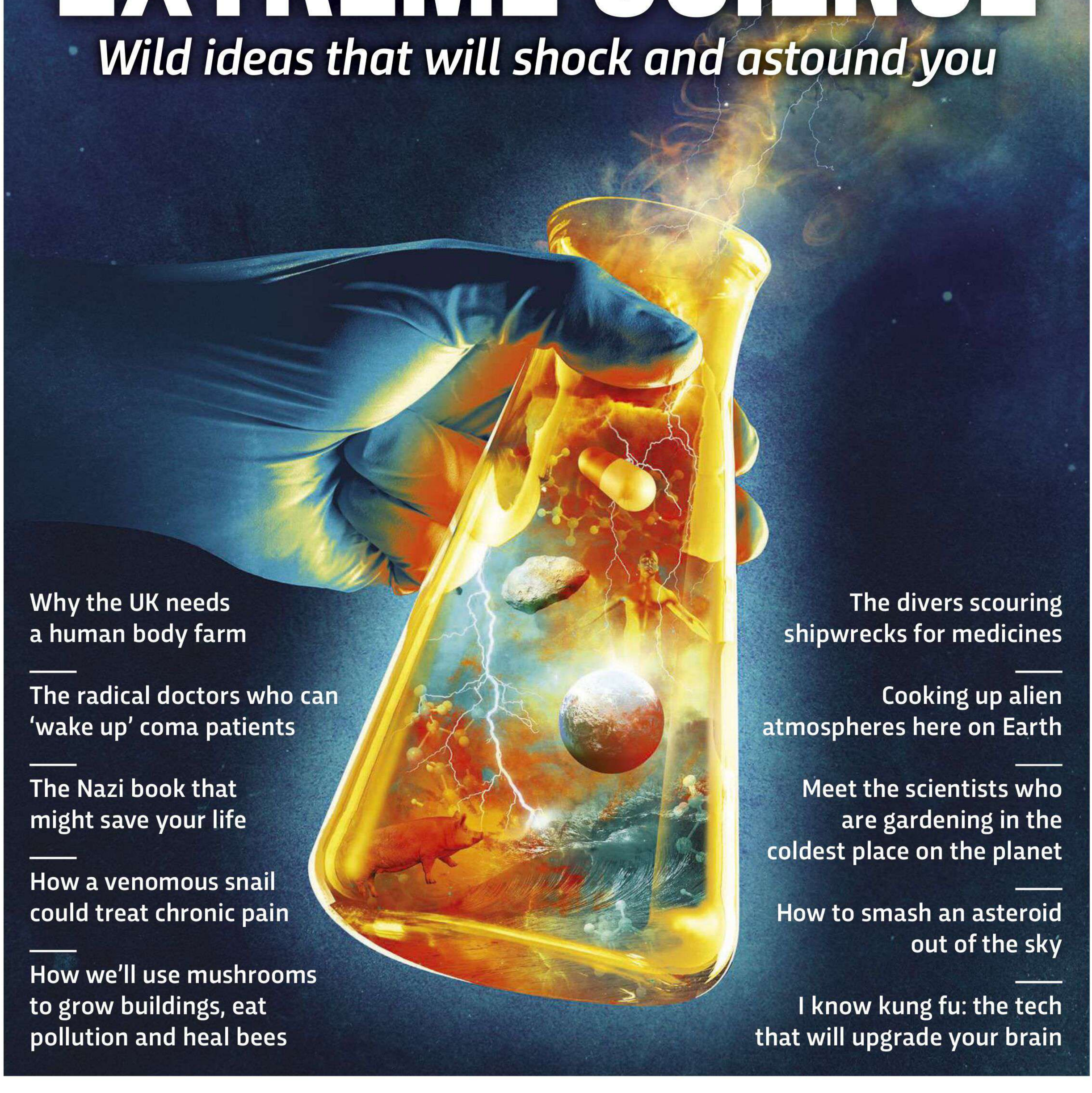

Why the UK needs a human body farm

The radical doctors who can 'wake up' coma patients

The Nazi book that might save your life

How a venomous snail could treat chronic pain

How we'll use mushrooms to grow buildings, eat pollution and heal bees

The divers scouring shipwrecks for medicines

Cooking up alien atmospheres here on Earth

Meet the scientists who are gardening in the coldest place on the planet

How to smash an asteroid out of the sky

I know kung fu: the tech that will upgrade your brain

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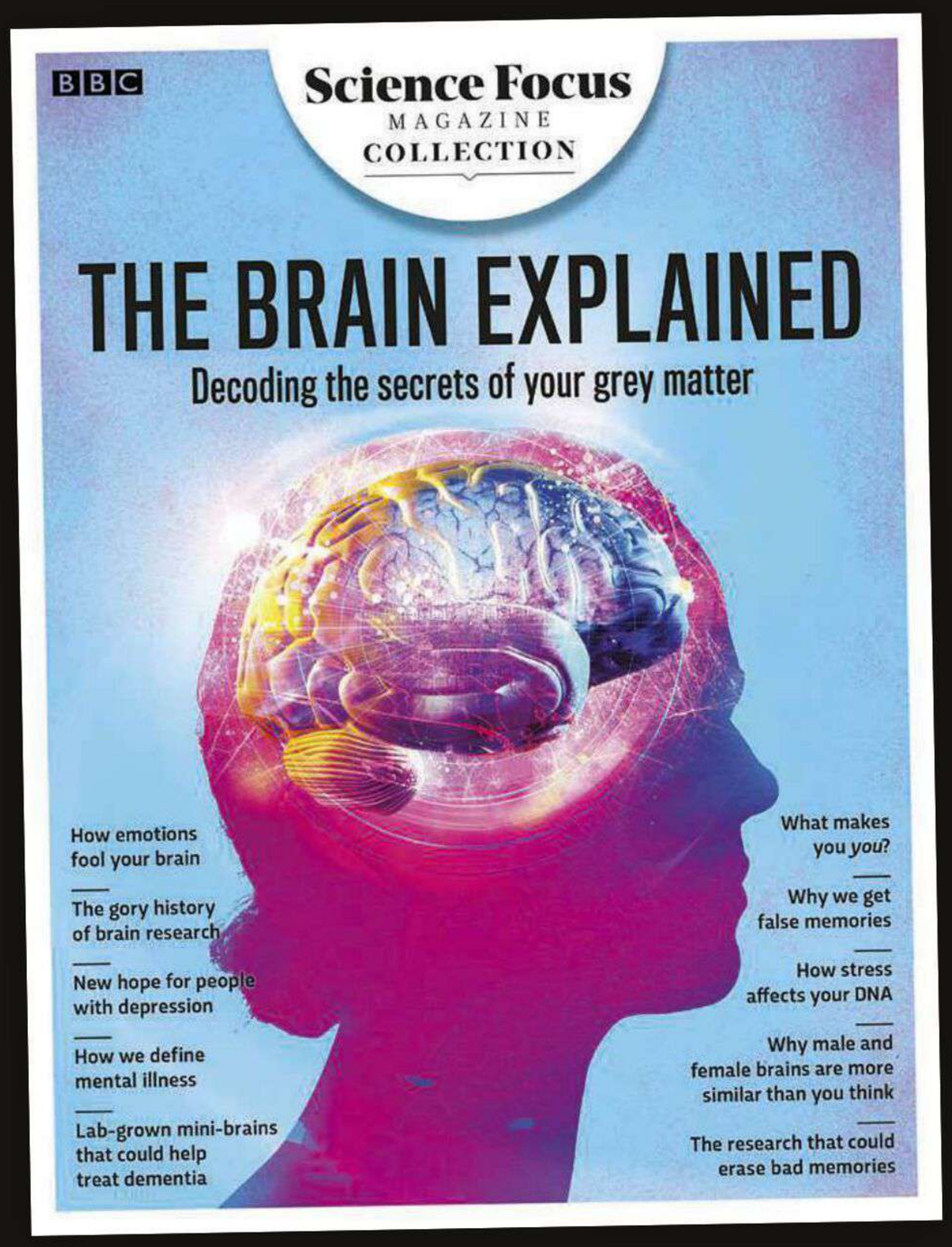
THE BRAIN EXPLAINED

Decoding the secrets of your grey matter



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IN THIS ISSUE...

- How **emotions fool** your brain
- What makes you ***you***?
- How to **build a brain**
- **The gory history** of brain research
- How we define **mental illness**

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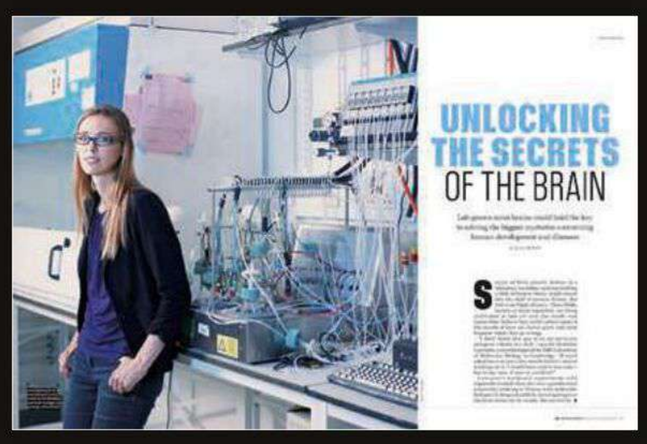

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COVERS: ANDY POTTS THIS PAGE: ALAMY

Welcome

Science can never be considered sluggish or uninspiring. In fact, it's a fast-moving field that offers unique ways to push the boundaries of what we know. By thinking laterally and trying new things, researchers in all disciplines, from astronomy to zoology, can discover cures for disease, understand the human mind, and even decipher the mysteries of the Universe.

So far, scientists have donned their scuba gear and plunged into lakes and oceans in order to hunt for new antibiotics that could help us treat disease (p48). They've also pulled on the protective gloves to milk some of the planet's most venomous creatures to find revolutionary compounds to target chronic pain, diabetes, cancer, multiple sclerosis and other conditions (p42).

For those who are more interested in the human brain, there has been some truly inspiring new science that could help us communicate with people in comas and even help bring them back (p38). Meanwhile, many people consider electroconvulsive therapy a violent treatment for mental illness, but doctors argue the modern way of performing the treatment is far gentler. With ECT centres closing around the UK, could we be losing a life-saving therapy (p20)?

Another taboo area is hallucinogenic compounds. Despite showing promise for treating mental health conditions, they became frowned upon as a field of study in the 1960s, thanks to their use by the counter-culture movement. But over time, the stance has softened and now it seems that – when combined with therapy – they can help with PTSD, OCD, depression, and could even offer ways to help us understand death (p26). Speaking of death, it's recently been announced that the UK will soon have its first 'body farm' where scientists can watch corpses rot. Feel that's a bit icky? I'm sure we can change your mind. Turn to p54 to find out why this is such an important step forward for forensics.

And some researchers are looking beyond our planet, too. We meet the team who are cooking up alien atmospheres right here on Earth (p74) to help us find out more about exoplanets. But some space scientists are feeling a little more destructive, and are going to unleash their inner Bruce Willis to smash an asteroid out of the sky and (maybe) avert Armageddon (p88).

Enjoy the issue!

Alice Lipscombe-Southwell, Editor

The deathstalker scorpion's venom is used to make tumour paint, which *only* sticks to cancer cells, allowing surgeons to see exactly what they need to remove

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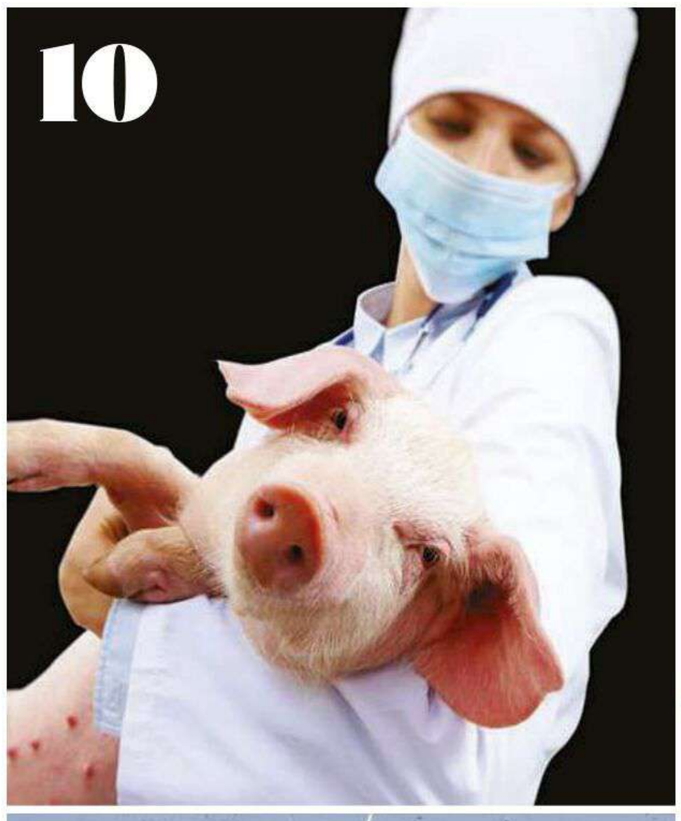

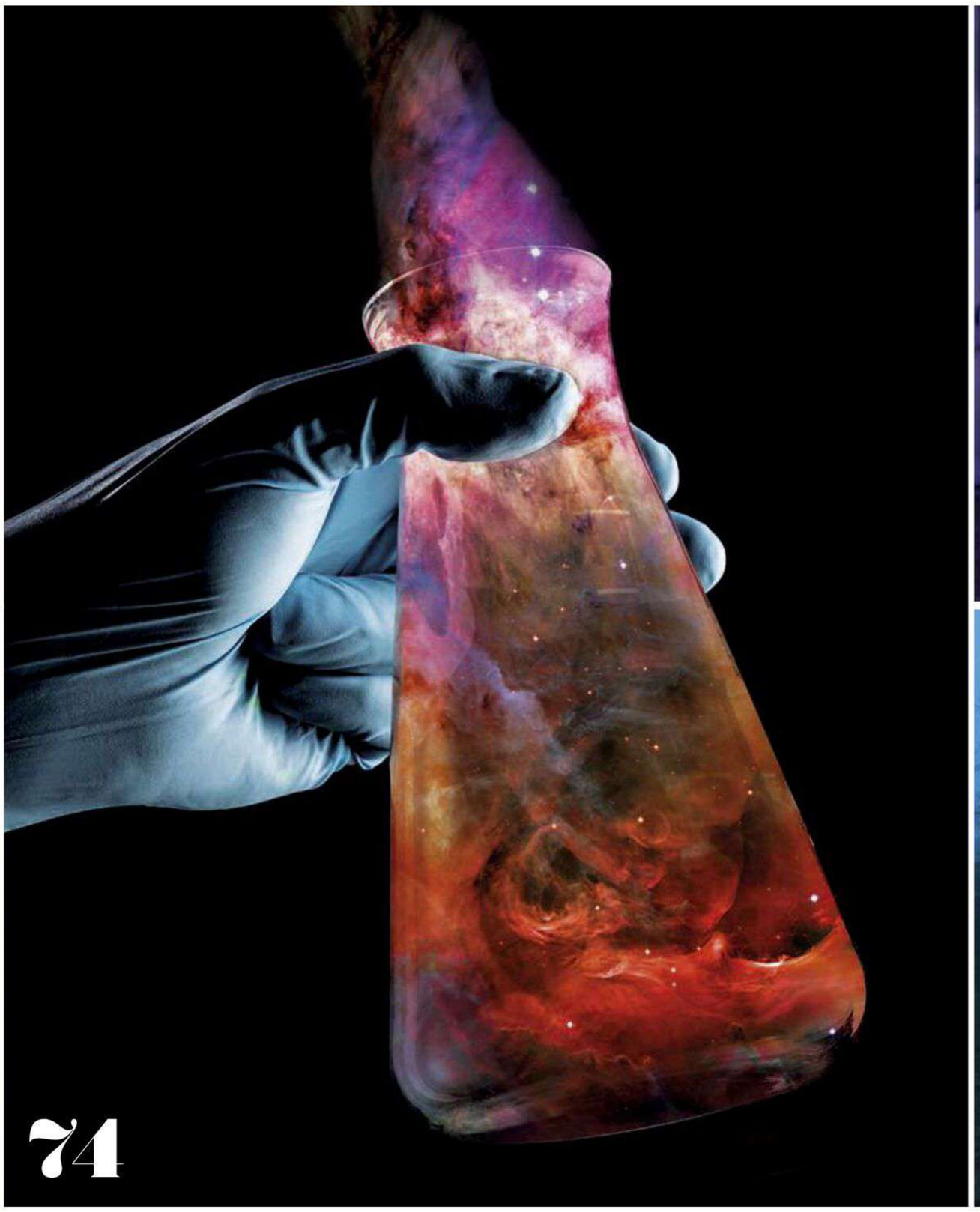

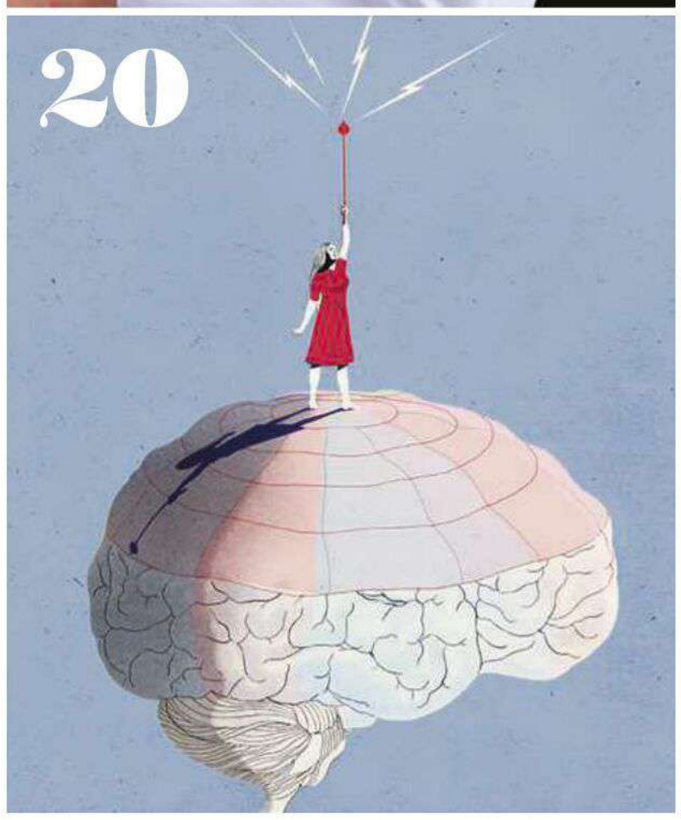

EYE OPENER

Cave raider

XINU ATTIC, CHINA

An intrepid explorer descends into the vast, murky depths of Xinu Attic, part of China's Er Wang Dong cave system. Their mission? To collect samples of microbes, from as deep as 500m underground. The expeditions are huge undertakings, but studying these microoganisms can reveal how they grow without light and with so few of the nutrients that would normally sustain life.

"The microbiology gets more interesting the deeper you get," explains microbiologist Dr Hazel Barton. "We'll spend around a week in the cave, exploring its structure and taking samples. We rig our own ropes, carry all our own camping gear and research equipment, sometimes through gaps as small as 20cm!"

Understanding the evolution and significance of the microbes living in these environments can help us better understand the cave itself and even its formation processes.

ROBBIE SHONE

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EYE OPENER

Saving our seas

SOCIETY ISLANDS,
FRENCH POLYNESIA

A diver takes notes as he monitors one of the coral nurseries in Mo'orea, French Polynesia. As the oceans continue to warm, primarily as a result of increased greenhouse gases from human activities, mass coral bleaching and disease outbreaks are becoming more and more frequent. Now, teams of marine biologists, including those from the Centre for Island Research and Environmental Observatory (CRIOBE) are working against the clock to repair and restore damaged coral reefs, by utilising 'resilient corals'. Using those corals not impacted by thermal stress, the team produce coral cuttings which are grown in a nursery and compared with other colonies to determine resilience capacity. In the longer term, it is hoped that projects like this one will help to reintroduce coral species to our reefs.

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XENOTRANSPLANTATION

Could a pig's heart save your life?

THOUSANDS OF PEOPLE ARE IN DIRE NEED OF A TRANSPLANT IN THE UK, BUT THERE JUST AREN'T ENOUGH DONATED ORGANS TO GO ROUND. SO SHOULD WE MAKE UP THE DEFICIT WITH ANIMAL ORGANS?

by MICHAEL REISS

Back in 2016 it was announced that researchers at the National Institutes of Health (NIH) in the US had kept a genetically engineered pig's heart beating in a baboon for three years. Though it was undoubtedly a headline-grabbing story, there are serious implications for the research. Every year, several million people die worldwide because of transplant shortages. There just aren't enough human organs from tragedies like road accidents to go around. But some scientists are working on a radical solution – to use organs from animals.

Xenotransplantation, as the procedure is known, may sound like something from a science fiction movie but doctors and scientists have been trying to develop it for decades. Back in 1984, Stephanie Fae Beauclair, generally known as 'Baby Fae', was born with a heart defect that would have killed her within a week or so. At that time, transplants using infant human hearts were nearly always unsuccessful. But her surgeon, Leonard Lee Bailey, was a pioneer in animal-animal transplants so decided to try transplanting a baboon heart. The hope was that it would allow Baby Fae to live long enough for a second operation to replace the baboon heart with a human one.

The surgery was initially a success, but Baby Fae died 21 days later when the heart was rejected by her body. Nevertheless, her sad story marks the first serious attempts at xenotransplantation. But 36 years on there are still many questions to be answered. Is xenotransplantation even feasible, and is it ethical?

INGENIOUS IMMUNITY

Our immune system is a wonderfully complicated collection of cells and organs that helps to protect us against any foreign bodies that invade and cause disease. Intruders, such as viruses or harmful bacteria, are attacked by highly specialised cells. Each of us has the physiological ability to recognise that our body and its organs are 'ours' and that invading objects are not. So while the white blood cells and other ▶

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components of our immune system attack foreign biological objects inside us, they do not attack us. The advantage of this is obvious: disease-causing organisms can be attacked and destroyed without the body turning against itself.

However, there is a serious downside when it comes to transplantation. The immune system can recognise the transplanted organ as foreign and attack it. To prevent this, patients receiving human-to-human transplants generally have to be given large doses of immunosuppressants to damp down the immune system and prevent it from attacking the transplanted organ. Unfortunately, patients with suppressed immune systems are less able to fight off germs, so they are more likely to catch infections. With a weakened immune system, even common diseases can prove very serious. However, this is less of a problem with the latest immunosuppressant drugs available.

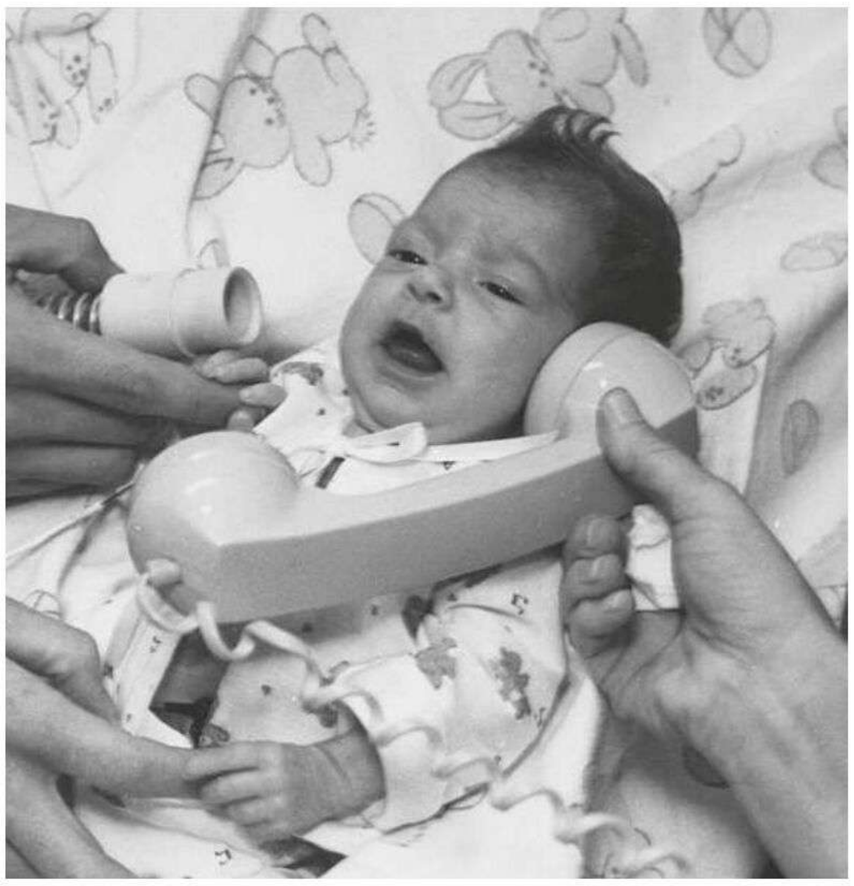
When it comes to transplanting non-human organs such as a pigs' hearts into humans, an extra difficulty arises. Within hours of the transplant, even if immunosuppressant drugs are used, so called 'hyperacute rejection' typically sets in and the transplant fails. In an attempt to overcome this problem, researchers are genetically engineering pigs to carry a single human gene that allows them to produce a human protein on the surface of their internal organs. It is hoped that this will trick the immune system into thinking the organ is human, therefore avoiding hyperacute rejection.

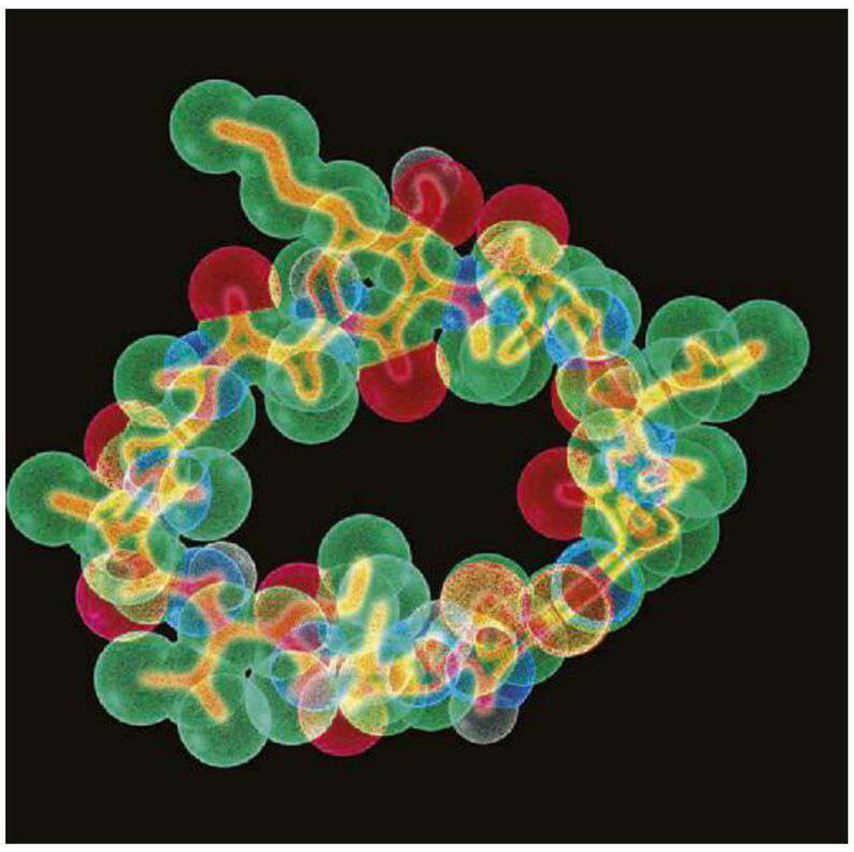
But rejection isn't the only problem that we face if we receive a transplant from another species. Pigs are the species of choice for human xenotransplantation. They are about the same size as we are, they are easy to keep in captivity and their physiology is surprisingly similar to ours, despite being less closely related to us than apes and monkeys. However, a lot of nasty human diseases result from viruses that come from animals. Pigs can carry as many as 50 porcine endogenous retroviruses, endearingly abbreviated to 'PERVs'. These are largely not harmful to the pig but can infect other species. This is what happened in 2009 when a pandemic caused by swine flu led to about 250,000 human deaths.

DO WE NEED XENOTRANSPLANTATION?

Each year tens of thousands of lives are saved as a result of human-to-human transplants. Indeed, the large majority of people waiting for a transplant never receive one. So what can we do about this?

The purchase of human organs – a market-led 'solution' to the shortage – is generally illegal. Iran, however, is one of the few countries that permits the sale and purchase of kidneys. As a result, the



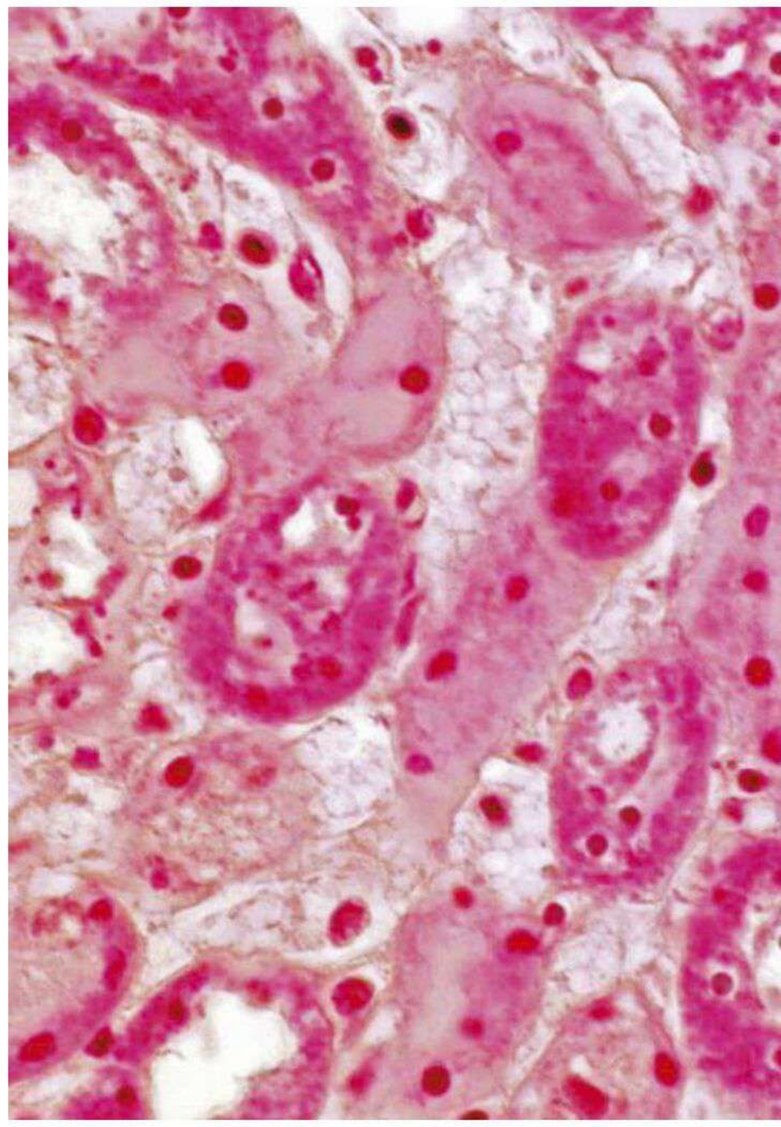


TOP 'Baby Fae' received a baboon's heart in 1984, but died 21 days after surgery when her body rejected the organ

ABOVE Immunosuppressants such as cyclosporin are taken by recipients of donated organs to reduce the risk of rejection, but they make the immune system less effective

ABOVE RIGHT Frederick West after receiving the UK's first heart transplant in May 1968; he died 46 days later from an infection, caused by weakened immunity

RIGHT Here, a rejected transplant kidney is filled with white blood cells (their nuclei can be seen as red dots), which have killed the foreign kidney cells



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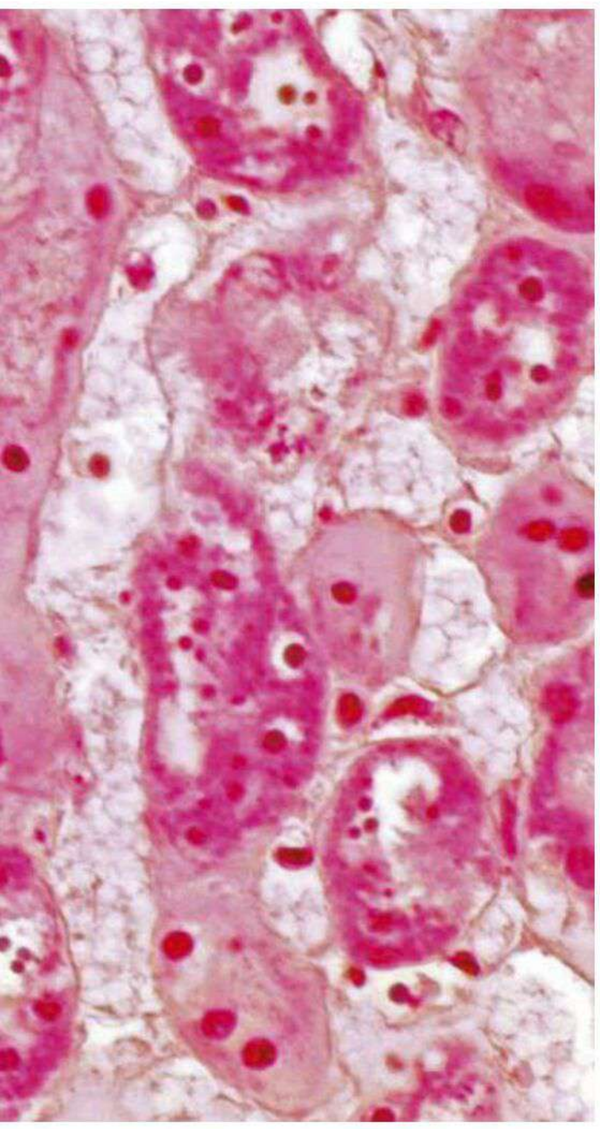


waiting times for kidney transplants in Iran are much shorter than elsewhere in the world. The going rate is about $4,000, if you are interested…

However, the primary reason why most people waiting for a transplant never receive one is that there simply aren't enough human organs to go around. There are several explanations for this. For one, the number of people who would benefit from a transplant continues to rise. This is partly because advances in transplant surgery mean that it is now possible to transplant more organs, and partly because an increasing range of medical conditions can now be treated by transplantation.

Another point to take into consideration is the fact that only a tiny proportion of deaths result in organs that are suitable for use in transplants. Deaths from motor vehicle accidents provide a high proportion of suitable organs. But thanks to improvements in road safety, the use of seat belts, improved car design, better roads, more speed limits, tougher driving tests and greater use of motorcycle helmets, the number of people killed in road accidents is falling.

A final issue is that some countries have some

"Iran is one of the few countries that permits the sale and purchase of kidneys. The going rate is about $4,000"

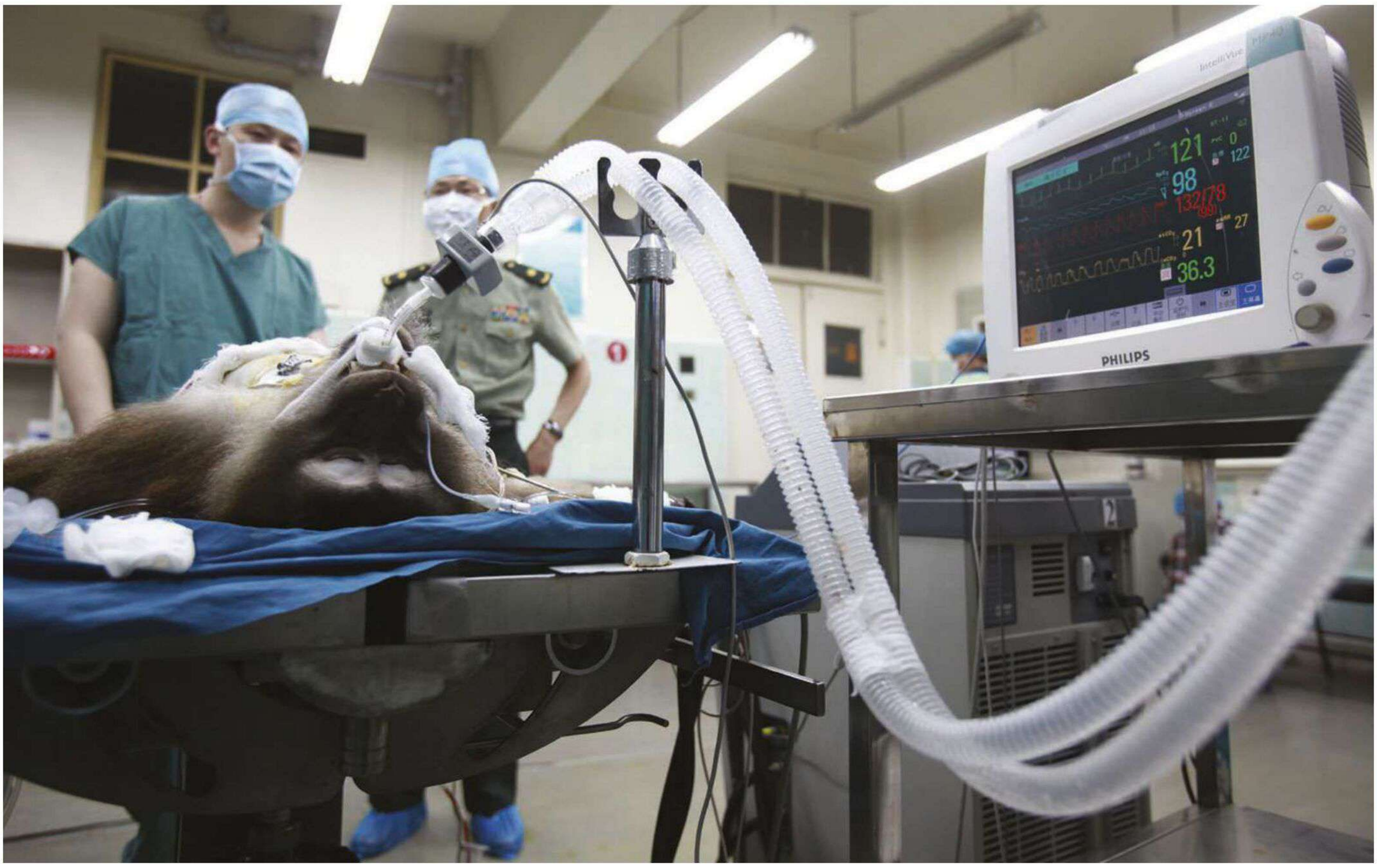
sort of 'opt in' rather than 'opt out' system for organ donation. This means that for a transplant organ to become available, the dead person needs to previously have expressed a wish for their organs to be used for transplantation – by carrying a donor card, for example – and doctors must also obtain the consent of the donor's relatives. However, organ donation law in England is changing, as the 'opt out' law will come into effect from 20 May this year.

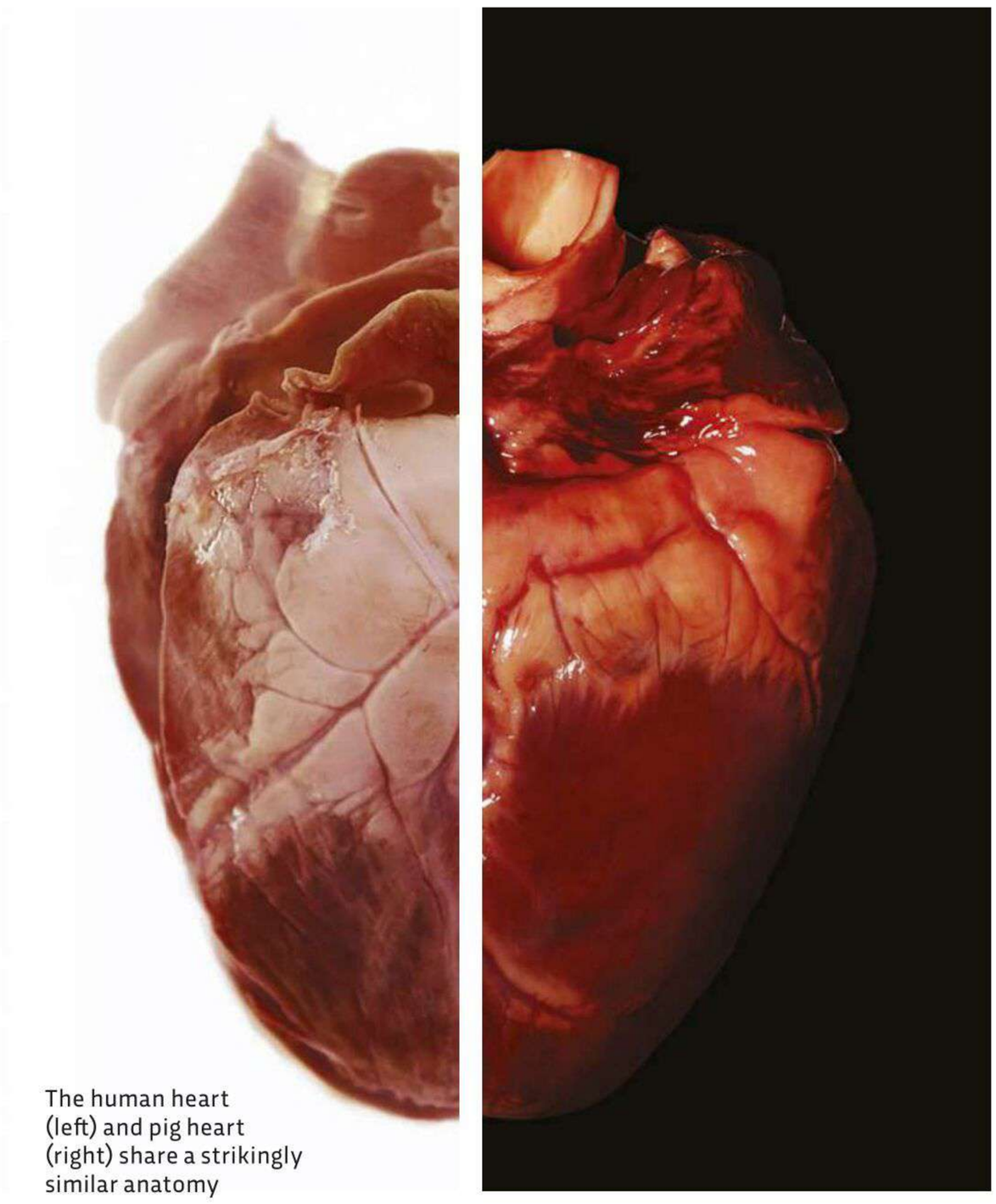
WHAT ABOUT WELFARE?

The extent to which animals can suffer is still argued, yet there is increasing acceptance that our closest evolutionary relatives have the necessary brainpower to experience suffering of some kind. A growing number of biologists and philosophers agree that, at the very least, the majority of mammals can suffer.

So would xenotransplantation lead to significant amounts of animal suffering? Consider, first of all, the pigs that are likely to be used. Companies involved in research on xenotransplantation maintain that their pigs are looked after extremely well. Indeed, in my experience, the animals used in the research are looked after better than pigs on most pig farms, in terms of the conditions in which they live. But there is more to the welfare of the pigs than their housing. For a start, the pigs used in the research are subjected to a number of surgical procedures. When clinical trials begin in earnest, it seems likely that 'gnotobiotic', or germ-free, animals will be needed. Such animals would probably be obtained by what is sometimes called 'surgical derivation'. This means that shortly before birth, the entire uterus with the piglets still inside would be removed from the mother. The piglets would then be raised in isolation and in sterile conditions. From the pigs' point of view, this doesn't sound like much of a life, as pigs are social creatures.

Furthermore, it is not only pig welfare that needs to be considered. Current research aimed at improving the success of xenotransplantation has meant that thousands of primates, including captive-bred macaques and wild-caught baboons, have already





The human heart (left) and pig heart (right) share a strikingly similar anatomy

been used in surgical operations as recipients of the transplants. When viewing many of these operations from the perspective of the scientists, surgeons, and ultimately the patients and shareholders who may benefit, many of these operations are deemed a research 'success'. From the point of view of the non-human primates, however, there's little doubt that these operations lead to considerable pain and a dramatic shortening of lifespan.

NATURAL VS UNNATURAL

Let us assume that xenotransplantation will require the genetic engineering of pigs through the insertion of one or more human genes into pig DNA. This involves changing the 'nature' of the pigs in at least some sense. Is this morally acceptable?

A frequent cry against genetic engineering of any sort is that it's 'unnatural'. However, this objection is difficult to defend. After all, what is 'natural'? Smallpox, tidal waves and death are natural, whereas vaccines, mobile phones and foreign holidays are not. In other words, in everyday language, there doesn't seem to be much of a relationship between what is 'natural' and what is good.

Even so, the 'unnatural' argument still has its defenders. A number of religions argue that, at least to some extent and in some sense, nature is good. In the Jewish and Christian traditions, the understanding is that on the sixth day "God saw everything that he had made, and behold, it was very

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"Some might condemn pig transplants on the ground that it is unpleasant or unnatural, but the alternative may be death"

ABOVE LEFT A macaque recovers after receiving a liver transplanted from a pig

ABOVE Pigs raised for xenotransplantation would probably need to be kept in a sterile environment, so would not be able to forage and play with other pigs

good". Death and decay entered the world through sin, but even after the fall of man, enough of God's goodness is present in the creation for much that is natural to be good. An entire theology of natural law has built up around this notion.

Nature is also seen as an indicator of goodness by many others, including those who do not follow any religion. To this day, there is a considerable body of opinion holding that 'natural' practices are preferable to their 'artificial' alternatives. Common examples include organic farming and the call to eat fresh rather than processed food.

Yet one great advantage of nature is that it has been around for quite a while. Consciously or otherwise, many of us think that our ancestors successfully brought up children, farmed and prepared food in 'natural' ways, so these traditional approaches must be okay. After all, and quite logically, one cannot be sure about the long-term consequences of any new technology, genetic engineering included, only of practices that have been around for a considerable time and are now considered 'natural'.

But does the type of genetic engineering really change the nature of pigs? From the pigs' point of view, it can be argued hardly at all. The practicalities of genetic engineering have significant welfare implications but it seems difficult to argue from a pig's perspective that the genetic engineering itself has changed its nature. The pig's behaviour is no different; its mental capacities and experiences are unchanged. The only difference is that it produces an extra internal protein. Traditional breeding, on the other hand, has resulted in incredibly significant changes to the natures of farm animals, including, for example, increased tolerance of high stocking densities, increased domesticity, and massive changes in milk, wool and meat production.

HOW WOULD YOU FEEL?

How would you feel about the thought of a pig's heart inside you? It is difficult to predict and would likely vary from person to person. Some people might condemn the idea on the ground that it is unpleasant or unnatural, but then the alternative may be death, which most of us don't like much either. It's worth noting that when human-to-human heart transplants were first introduced, some commentators said that they were deeply immoral. Yet we rapidly got used to the idea of human-to-human transplants, and most people on the receiving end are deeply grateful for them. Could we see the same thing with xenotransplantation? Only time will tell. **SF**

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by **MICHAEL REISS**

Michael is professor of science education at UCL and a priest in the Church of England. He has advised the House of Lords on the use of animals in scientific procedures and was the ethicist on the Farm Animal Welfare Committee (FAWC) from 2004 to 2012.

Nazi scientists developed a system of human and ape facial measurements to establish racial descent. They used biased results to back up their claims that Aryan Germans were more evolved, while Jewish people were closer to apes

FORBIDDEN MEDICINE

FROM NAZI MEDICINE TO GM BABIES, UNETHICAL RESEARCH HAS A DEEPLY PROBLEMATIC HISTORY. BUT WHAT SHOULD WE DO WHEN THE RESULTS OF THESE STUDIES COULD OFFER USEFUL SCIENTIFIC INSIGHT?

by TOM IRELAND

More than 30 years ago, in 1988, hypothermia expert Robert Pozos decided to unearth a document that society had tried to forget for almost 40 years. The 68-page report, compiled by an American army officer after WWII, contained details of the horrific experiments that Nazi doctors had conducted on many people in concentration camps.

These procedures, and the conduct of the Nazi doctors stationed at camps such as Dachau and Auschwitz, make for difficult reading. More akin to sadistic torture than research, the 'experiments' involved Jews being frozen to death, dissected alive, poisoned, wounded without anaesthetic, or sterilised – all supposedly in the name of advancing Nazi medicine.

After the details of Nazi war crimes were revealed at the Nuremberg Trials in the late 1940s, the documents relating to these atrocities were placed in the US Library of Congress. It was imagined that few would ever want to take such material off the shelves.

Yet Pozos, the director of a hypothermia research lab at the University of Minneapolis, believed the results of some of these evil studies could be used for good. He thought that the Nazi experiments on the effects of cold – conducted in the hope that it might help downed German fighter pilots survive longer in freezing waters – could be useful in his work developing treatments for severe hypothermia.

The Nazis had meticulously recorded the effects of cold up to the point of death, and trialled various methods of warming people up from the brink. It was the sort of data Pozos could never obtain with volunteers or patients in a trauma ward. It could help save lives. To some, the plan to use Nazi 'research' was an outrage. How could one treat accounts of human torture as if it were scientific data? Yet others, including some relatives of the victims, felt that if it meant some good could come from such terrible suffering, then it should be done. The dilemma kick-started an ethical debate that still divides opinion today: what should we do with the results of tainted or unethical research?

Pozos was not the only person who wanted to access and analyse the Nazi research. Around the same time another hypothermia expert, John Hayward, went ahead and used results from Nazi experiments to help develop survival suits for fishermen working in freezing waters. And in 1989, the Environmental Protection Agency (EPA) in the US urgently needed to understand how phosgene gas affects humans. Phosgene is an important industrial chemical that's used in the production of certain plastics, but the EPA found there was barely any research on the subject of its toxicity in humans – except in Nazi literature.

"IF SOME GOOD COULD COME FROM TERRIBLE SUFFERING, THEN IT SHOULD BE DONE"

The Nazis had gassed French soldiers with phosgene to record its ghastly effects; most of the prisoners died slow, painful deaths. With many US communities living near phosgene production plants, and amid rumours that Saddam Hussein was planning to use phosgene weapons on US soldiers, the EPA was forced to consider using the Nazis' murderous study in their assessment. Eventually, they backed down amid protests.

So, if good can come from an unethical experiment, should we use it? "There are two main concerns when considering whether to use this kind of data," says Dr Sarah Chan, a medical ethics expert at the University of Edinburgh. "Firstly, does it somehow make us complicit in the wrong that happened if we use it? And secondly, by using ➤

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it, are we legitimising or encouraging this behaviour in the future?"

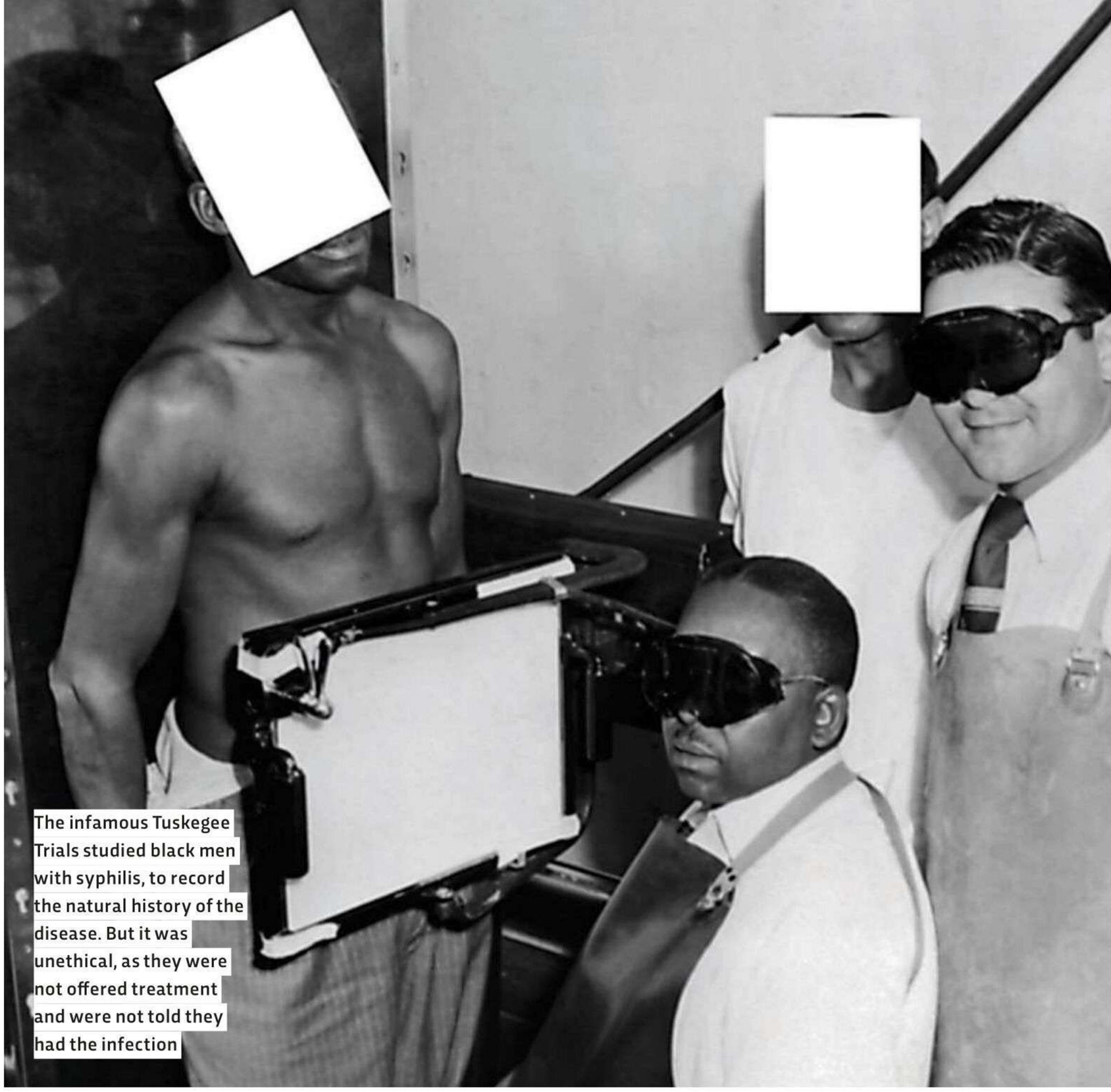
Chan believes that if people are sure that the answer to those two questions is no, then the use of results from tainted research can sometimes be justified.

"I think there are good arguments on both sides," says David Reisnik, a bioethicist at the US National Institute of Environmental Health. "In some cases, the data could be valuable for public health or advancing scientific research – but on the other hand it sets a bad precedent that data from unethical experiments will still be used. There are people who say you shouldn't use it, no matter what potential good could come from it, to send the message that ethics are important and should not be violated."

TOUGH DECISIONS

While Nazi experiments mark a low point in the history of medical research, many great advances in medicine were built on the back of research that seems completely unacceptable by modern standards. Early anatomists in England and Scotland, for example, faced a shortage of cadavers to use in their studies due to the regulations of the time. Many, including the great physician Robert Knox, learnt how the human body worked by studying corpses stolen from graves or even killed to order by the infamous murderers William Burke and William Hare. Edward Jenner, the country doctor and pioneer of vaccination, deliberately infected his gardener's son with cowpox as part of his early studies. Jenner's work is said by some to have saved more lives than any other experiment in history, and earned him a medal from Napoleon. A similar experiment today might earn him a prison sentence.

In both cases, the huge strides forward that resulted from terrible scientific practices cannot realistically be ignored or undone. Despite efforts to formalise the law around human experiments following WWII, shameful practices continued throughout the rest of the 20th Century. In the 1960s, the paediatrician Saul Krugman deliberately infected children who had intellectual disabilities with hepatitis in order to study how the disease spread. (He said the children's home where he conducted the study was so rife with the disease they "would have got it anyway", and was awarded several awards for his work.) During the infamous Tuskegee Trials, run by US health agencies, black men with syphilis were studied for decades without being offered treatment so that researchers could see how their disease progressed. It was not until the 1970s that the trial was finally shut down.



The infamous Tuskegee Trials studied black men with syphilis, to record the natural history of the disease. But it was unethical, as they were not offered treatment and were not told they had the infection

"THE DEFINITION OF 'ETHICAL' AND 'UNETHICAL' IS CONSTANTLY SHIFTING"

Chan believes that if society can use the results of tainted research without giving credit or credibility to those who conduct it, it could help reduce the lure of notoriety that attracts some people to act unethically. "If we think about what motivates people to engage in research we deem unethical, part of it must be that no matter how history condemns them, they will be known as 'the first person to...' or 'the author of'. It's about recognition. So we should think about how to use this knowledge without glorifying the acts that led to it."

Recently, there seems to have been a rise in research deemed to be unethical. An example is He Jiankui, the Chinese biologist who shocked the world in 2018 by announcing he had helped create the first ever genetically-modified babies – twin girls born from embryos he had modified using the gene-editing tool CRISPR. Scientists around the world had previously agreed that the technology was not ready to be used in this way. As well as crossing many ethical and regulatory red lines, Jiankui did

ALAMY, GETTY IMAGES, SCIENCE PHOTO LIBRARY

There was widespread outrage when Chinese scientist He Jiankui announced he had helped create GM babies in 2018, but his work still made headlines

not even publish his results. He simply posted a video about what he'd done to YouTube. His work still made headlines worldwide.

"The reality we have to deal with is that the dissemination of science now goes far beyond traditional academic publishing," says Chan. "No matter what we do to say 'you will not be credited, you will not be published in academic literature, we will not cite this research', the world at large still knows it has happened and wants to know if it worked."

SHIFTING DEFINITIONS

What makes things even more complex is that the definition of 'ethical' and 'unethical' is constantly shifting. Chan thinks it is important to consider what the scientific community deemed acceptable at the time the research was done. "If you do something wrong and at the time all your peers were also doing it and agreed it was okay, it is still wrong, but it is less wrong than doing something where all your peers are saying 'don't do that, it's horrific,'" says Chan. "There is an extra wrong in flagrantly breaching the standards of your community."

Reisnik, meanwhile, says it is likely that research we consider as ethically sound today could be viewed differently in future. "Just in my lifetime there have been huge changes in how human biomedical data is handled. It was routine to take tissue specimens for surgeries, use them in research and not tell people what they were doing," he says. "I don't know what the ethical issues of the future might be, but it is getting easier and easier to re-identify tissue and genetic data that we thought were completely anonymised. It's quite possible things will change, and what we think is okay today might not be considered okay 100 years from now."

Ultimately, when it comes to research that could save lives but comes from a terrible source, it can help to put yourself in the position of a person whose life depends on having the best information available. The BBC recently reported how lots of surgeons still use a book of anatomical illustrations produced by a Nazi physician, because it is considered to be one of the finest anatomical guides to the human body ever produced. *The Pernkopf Topographic Anatomy Of Man* was drawn using the corpses of people killed by the Third Reich, yet doctors want access to the best material to guide their work.

"If I was about to head into surgery," says Chan, "and I knew that I would have a better chance of survival if my surgeon could refer to this book, I would want them to refer to it."

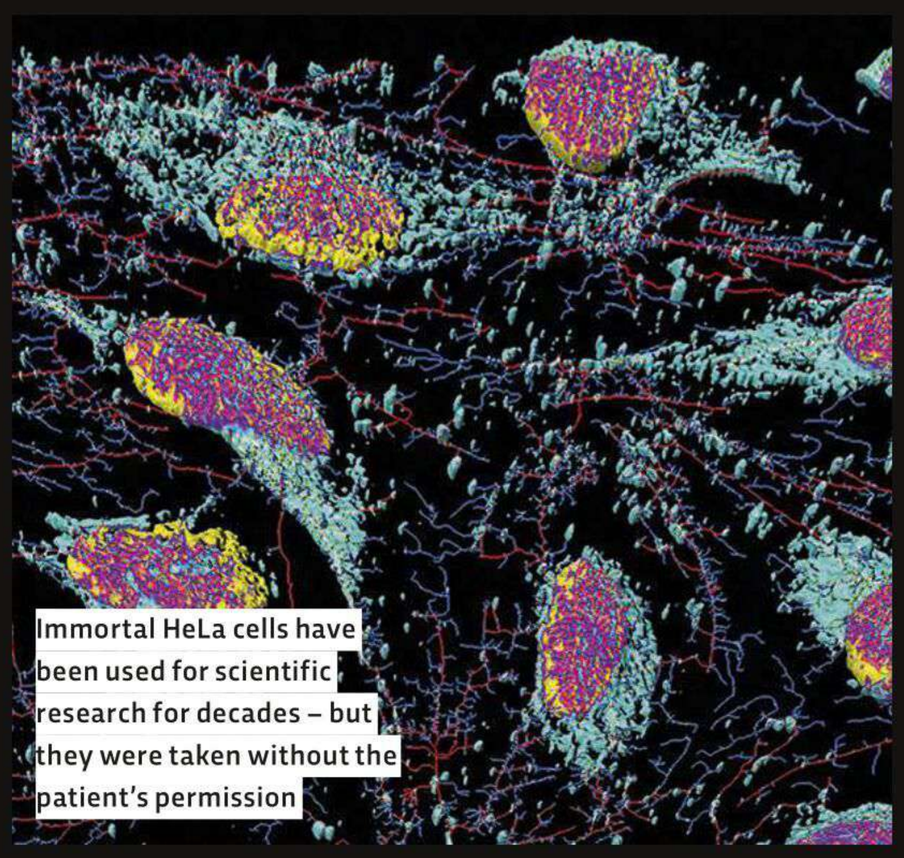
Would you? **SF**

by **TOM IRELAND**
(@Tom_J_Ireland)
Tom is editor of The Biologist *at the Royal Society of Biology.*

Who do HeLa cells belong to?

In 1951, a young black woman called Henrietta Lacks was treated for cervical cancer at Johns Hopkins Hospital in Baltimore, Maryland. As was common at the time, especially for black or poor patients, she was not told that the tissue from her biopsy might also be used for scientific research. Her cells turned out to be unlike anything doctors had ever seen: they grew quickly and could be kept alive outside the body, seemingly indefinitely. This remarkable 'immortalised' cell line (known as 'HeLa' after Henrietta Lacks) meant scientists could conduct detailed, long-term studies on human cells in the lab for the first time. Lacks died shortly after her biopsy was taken, and her family were not told about the HeLa cell line, even as it developed into a valuable (and profitable) scientific resource. The cells have been central to many important biological studies for almost half a century. It is only recently that bioethicists have started to address the questions raised by the case around consent, privacy, racism in research, and the ownership of biomedical data.

Today, regulations governing the use of human tissue and genomic data are far stricter, and Lacks's family has since become involved in decisions around the use of HeLa cells. But is it right that scientists around the world are still keeping cells descended from this woman alive, without her permission, years later?



Immortal HeLa cells have been used for scientific research for decades – but they were taken without the patient's permission

SHOCK VALUE

Electroconvulsive therapy has a reputation as a violent – even barbaric – treatment for mental illness. But with clinics gradually closing nationwide, is the UK losing a life-saving therapy?

by HELEN GLENNY

On a cold Monday in May 2010, Karen escaped, in a panic, from her room in a Birmingham hospital's psychiatric ward. She arrived at a motorway flyover. Looking down, she watched the traffic, plotting for the perfect time to jump. The flashbacks had become too much. "My only purpose was to end my life," she recalls. "I did not want to be here."

Karen's descent into severe depression had started six months earlier, when her husband had been diagnosed with a life-threatening heart condition and she had dedicated herself to supporting him and their three kids. Her partner recovered and returned to work, but Karen began to struggle psychologically, and in the months that followed she isolated herself from her friends, became anxious and eventually stopped eating. After losing a dangerous amount of weight, Karen saw a psychiatrist, who admitted her to hospital.

Everyone thought the stress of her husband's illness was the sole cause of Karen's downward spiral, but it wasn't that simple. "Things came back that I'd been burying," she says. "I wasn't able to bury them any more." During an appointment with her psychiatrist in hospital, Karen spoke for the first time about a traumatic event from her childhood. When she was 14, she had been raped by a stranger on her way home from a friend's house. "I didn't tell anybody about it. It was a form of self-protection: if I didn't talk about it, it hadn't happened," she says.

After that revelation, flashbacks plagued her. "It was like going through it all over again, what I could feel, what I could see, what I could hear," says Karen. A week after that meeting with her psychiatrist, she took a step up onto the flyover's protective metal railing, ready to jump. Within seconds, two passing drivers pulled over, got out of their cars, and prevented her from jumping for long enough for the police to arrive and take her back to hospital.

BEYOND THE SHOCK

In the past year, more than 18,000 people have been hospitalised in the UK with depression. Many of those people have a severe, treatment-resistant form of the illness, meaning they haven't had any success with the usual treatments, like psychotherapy and antidepressants.

Some UK psychiatrists choose to offer these patients a treatment that's clouded in stigma and believed by many to be barbaric and ➤

ILLUSTRATION: EMMANUEL POLANCO

abusive: electroconvulsive therapy, or ECT. In 2016-17, around 1,700 people received ECT in England, Ireland, Wales and Northern Ireland. During the treatment, an electric current is passed through a patient's brain to induce a seizure. Proponents of ECT claim that it is the fastest acting and most effective treatment for severe depression, and argue that the stigma prevents patients from receiving a potentially life-changing therapy. One of those psychiatrists was looking after Karen in December 2010, seven months after her first suicide attempt, and saw the possibility of an effective treatment when nothing else she had tried had helped.

A modern ECT session, says Prof George Kirov, a psychiatrist at Cardiff University's School of Medicine, goes like this: an anaesthetist inserts a thin tube in the back of the patient's hand and administers both muscle relaxants and a general anaesthetic, which puts the patient to sleep. An ECT nurse squeezes conductive gel onto a pair of electrodes and holds one to each of the patient's temples. Another member of the team then sets the level of the electrical current, and pushes a button. Current pulses briefly through the electrodes, eliciting a seizure that lasts between 15 and 40 seconds. Prof Rupert McShane, a consultant psychiatrist at Oxford Health NHS Foundation Trust, explains that the muscle relaxants keep the patient mostly still. "Usually you can see some muscle twitching, but we use an electroencephalogram [which monitors brain activity] to see that the patient is having a fit."

The procedure is surprisingly quick. The patient wakes up a couple of minutes after their seizure finishes, and they are taken to a supervised recovery room. When they feel up to moving, they are offered a drink and some food. They'll do this twice a week, for around six weeks.

After Karen's first session, in December 2010, she woke up to "the worst headache of my life", she says. Other patients report becoming confused and needing time to remember where they are. During the weeks of treatment, patients often experience memory loss; for the majority, this resolves itself in the months after treatment finishes.

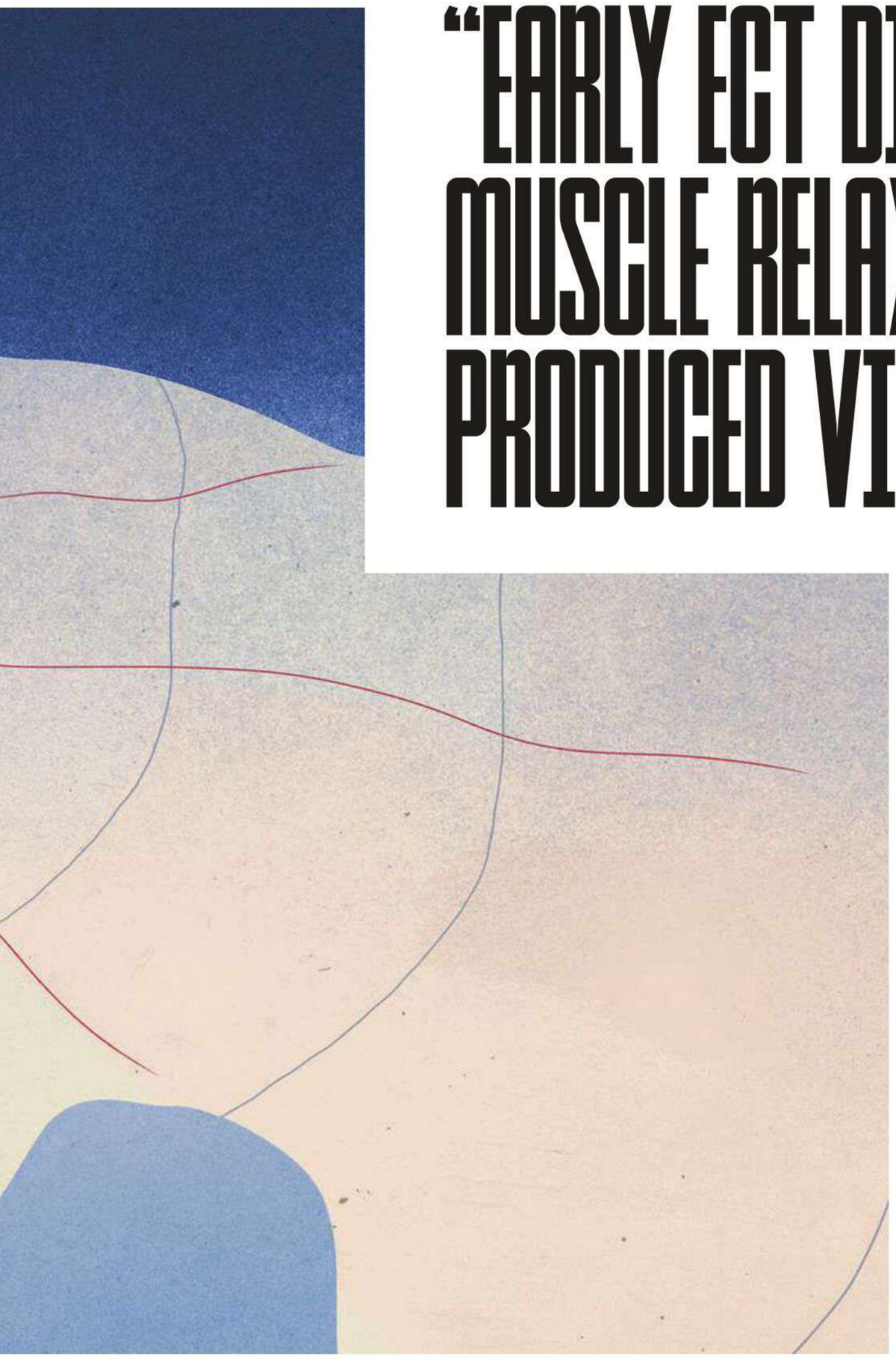
After her fourth session, Karen went back to her ward and asked for a drink. This was a big deal for two reasons. Karen had lost any interest in eating or drinking over the preceding weeks – now she was doing it voluntarily. She had also chosen to speak to someone – another rarity. With each session she felt progressively better, and eventually started eating on her own. "It felt like there wasn't something heavy on me any more," she says. Karen stopped after nine sessions, and her psychiatrist discharged her a few weeks later, in February 2011.

THE SCIENCE

What was going on in Karen's brain that made her feel better so quickly? No one knows, exactly. What we do know is that the seizure is key: the better the seizure – gauged by certain

68

The number of ECT clinics that have closed in England, Wales, Ireland and Northern Ireland since 2009.



"EARLY ECT DIDN'T USE MUSCLE RELAXANTS, SO IT PRODUCED VIOLENT SEIZURES"

qualities on the EEG – the greater the improvement. Researchers have found several possible pathways that could be involved (see box, overleaf).

Karen's rapid response was not unusual, however. In 2004, results from one of the largest ever ECT studies were published in the *Journal Of Clinical Psychiatry*. The study looked at 253 patients with major depressive disorder, and found that three-quarters of them reached remission after receiving ECT. In this context, remission can mean that mute patients start speaking, or catatonic patients start moving. Suicidal thoughts might recede, and patients may begin to engage with long-term therapy. McShane says that, for people with severe depression, those rates of improvement are considerably better than for antidepressants. But ECT research isn't without controversy.

Clinical psychologist Dr John Read at the University of East London points out that no placebo-controlled study of ECT has been published since 1985, and those published before then were of "questionable methodological quality". Without trustworthy placebo-controlled studies, he says, any positive ECT results could simply be due to a placebo effect. In contrast, McShane says that the pre-1985 studies have already proved ECT's effectiveness, and cautions against repeating those studies: "It would be unethical to take a group of people with depression and treat half of the sample with an ineffective, sham treatment."

Read also has concerns that the effect of ECT doesn't last, and claims there has never been a long-term follow-up study in which ECT outperforms a placebo. And indeed, Kirov notes that in his clinic, and in others in the UK, about half of patients become unwell again within a year. This is even with the help of antidepressants, psychotherapy and what's called 'maintenance ECT', where the patient continues with ECT, but with decreasing frequency. Kirov says that relapse is ECT's biggest problem. "They get back into depression. Not necessarily to the same level, but they go back." And if relapse is the main problem with ECT, then side effects are certainly the second.

In 2011, the late actor Carrie Fisher wrote about her experience with ECT in her memoir *Shockaholic*. But her mostly positive account came with a caveat: "The truly negative thing about ECT is that it's incredibly hungry and the only thing it has a taste for is memory."

ECT interferes with memory, both anterograde (the laying down of new memories), and retrograde (recalling things from the past). Anterograde memory problems usually resolve themselves a few months after finishing treatment, but for some individuals – 13 to 55 per cent of people, depending on which study you read – retrograde memory loss can be permanent. Kirov says that for these people, continuing becomes a personal choice: "Some of them are disturbed by their memory problems and decide to stop." Karen experienced retrograde memory loss, though it has improved since finishing treatment. "I couldn't remember things, like what we did on holiday, and that was quite frustrating. But I didn't like being unwell, so there was a trade-off."

REPUTATION PROBLEMS

Historical scars also mar ECT's reputation: early applications didn't use muscle relaxants, so it produced violent seizures where patients occasionally broke bones. Ken Kesey's 1962

ILLUSTRATION: EMMANUEL POLANCO

HOW DOES ECT WORK?

RESEARCHERS HAVE DISCOVERED SOME CHANGES IN THE BRAIN AFTER ECT, BUT HAVEN'T SETTLED ON ANY DEFINITIVE ANSWERS AROUND HOW IT WORKS. HERE ARE THE MAIN CONTENDERS...

HORMONES AND NEUROTRANSMITTERS IN THE BRAIN

ECT increases the levels of some neurotransmitters (chemical messengers that transmit signals between neurons) and hormones in the brain. Serotonin and dopamine are two neurotransmitters that increase after ECT. Serotonin regulates anxiety and reduces depression, while dopamine affects mood and motivation. Antidepressants have similar effects on the brain, but as ECT is generally faster acting and more effective than antidepressants, experts believe these changes cannot entirely account for ECT's benefits.

INCREASES IN THE SIZE OF THE BRAIN'S EMOTIONAL PROCESSING AREAS

A recent study in humans showed that ECT increases the amount of grey matter in the brain's hippocampus and the amygdala.

The hippocampus is involved in learning, memory and emotion, while the amygdala plays a role in the processing of emotions. However, this increase in volume of grey matter wasn't correlated to noticeable changes in the mood of the patients, so more research is needed to establish whether or not this is a contributing factor.

CHANGES IN BRAIN CONNECTIONS

One study has shown that patients with severe depression have more connections between certain brain regions, including the prefrontal lobes, than healthy controls. Experts suggest that these connections could account for the ruminations and hyper-alertness that characterise some forms of depression, so decreasing these connections might help a patient. According to several studies, after ECT there are fewer connections between prefrontal lobes and other areas of the brain. But ECT may also build new connections in some areas of the brain, so more research is needed.

book *One Flew Over The Cuckoo's Nest*, and the 1975 movie, depicted ECT as a form of behavioural control for psychiatric patients, perhaps an accurate portrayal of certain hospitals back in the 1950s. And in the 1980s, ECT was used as a 'treatment' for homosexuality. This practice didn't last, but it still remains etched in cultural memory.

"THERE IS A ROLE FOR ECT. BANNING IT WOULD BE LIKE REMOVING A LIFELINE"

The use of ECT is declining in the UK, according to the latest report by the ECT Accreditation Service. "Its portrayal in movies has been profoundly stigmatising, and has misrepresented current practice," says McShane. He argues that a lack of knowledge around severe depression means the costs and benefits of the treatment cannot be accurately weighed up. "That discussion often omits the severity of the illness. ECT causes side effects, but so does chemotherapy." He says that if the public were more aware of the reality of being severely mentally unwell, they might be more accepting of the treatment – "but those patients often don't want to talk".

Stigma can affect doctors as well as patients. According to Kirov, most psychiatrists who object to ECT haven't actually seen it used. To counter misinformation, he encourages every medical student to observe ECT. But he isn't sure what to do for the public. "It's hard to change public opinion. People have heard too many bad stories," he says.

To make matters worse, ECT has become a proxy for a long-argued question: is depression a medical problem, or a social one? Read, who's critical of ECT, argues the social side, saying that ECT is the most extreme example of the over-medicalisation of human distress: "It's not an appropriate response to a social problem." He calls for more work on population-wide wellness, and improved access to a range of psychological therapies and social support. McShane insists that ECT patients "are generally either too ill to make use of psychotherapy, or have already tried it without success".

BRIGHT FUTURE

In the end, Karen needed both ECT and psychotherapy. Her return to health was difficult. She relapsed a few months after her first course of ECT, falling back into severe depression. "I was reliving [the trauma] all the time. I started hearing him constantly talking to me, and I could feel him touching me." By February 2012 she was back in a psychiatric unit, sectioned after another suicide attempt. She spent a year and a half trying various other therapies, before starting her second round of ECT in August 2013. At that time, Karen was too unwell to give consent herself, but her family fought for her to receive it.

After three sessions, Karen became calmer. "I had lots of input from then on," she says. Karen was assigned a new psychologist, who guided her through psychotherapy during her ECT. She continued with the ECT, gradually reducing its frequency, until she was having just one session every three weeks. In September 2014, she was discharged, and in 2015 decided to stop ECT completely. "I'd got to a point with therapy where I was processing what had happened to me," she says. In 2016, after three years of therapy, Karen decided to stop that too. She doesn't regularly see doctors any more, and says that life is finally back to normal for her.

What would have happened if ECT wasn't an option? "I don't think I'd be here," she says. She cautions that while ECT certainly isn't for everyone, "there is a role for it. Banning it would be like removing a lifeline." **SF**

by **HELEN GLENNY**

Helen is a freelance science and travel journalist, with a background in neuroscience and physiology.

DISCOVER MORE

BBC three

Watch short films and read articles about mental health from the BBC Three series Minds Matter. ***bit.ly/bbc_mind_matters***

If you have been affected by any issues raised in this article, there is help and advice available here: ***bit.ly/mental_health_support*** *If you are concerned about the mental health of you or a loved one, please visit your GP.*

ILLUSTRATION: EMMANUEL POLANCO

TO DEATH AND BACK

No one can give a first-person report on what it's like to die, but near-death experiences and drug trips could offer us a glimpse beyond the veil

by DR CHRISTIAN JARRETT

What is it like to die? In 2012, the retired US neurosurgeon Eben Alexander reassured us in his book *Proof Of Heaven* that it is a blissful experience. Of course, he wasn't speaking from beyond the grave. His claims were based on what he said had happened to him during a week-long coma a few years earlier. While close to death and with his *E. coli*-infected brain rendered virtually inactive, Alexander said he had a transformative experience that included travelling through a black void "brimming over with light: a light that seemed to come from a brilliant orb". He also described being comforted on his journey by a young woman with high cheekbones and blue eyes, who told him he had nothing to fear and that he was "loved and cherished, dearly, forever".

Alexander's fantastical account divided opinion. Millions rushed to buy his book, and the US magazine *Newsweek* splashed his story on their cover with the headline "Heaven is real". Yet eminent neuroscientists such as Sam Harris and Colin Blakemore queued up to pick holes in the account and to present a more biologically grounded version of events. "Of course, the brain does funny things when it's running out of oxygen," wrote Blakemore at the time. "The odd perceptions are just the consequences of confused activity in the temporal lobes."

WARNING

LSD, DMT and psilocybin are Class A drugs according to UK law. Anyone caught in possession of such substances could face up to seven years in prison, an unlimited fine, or both.

Information and support for those affected by substance abuse can be found at **bit.ly/drug_support**

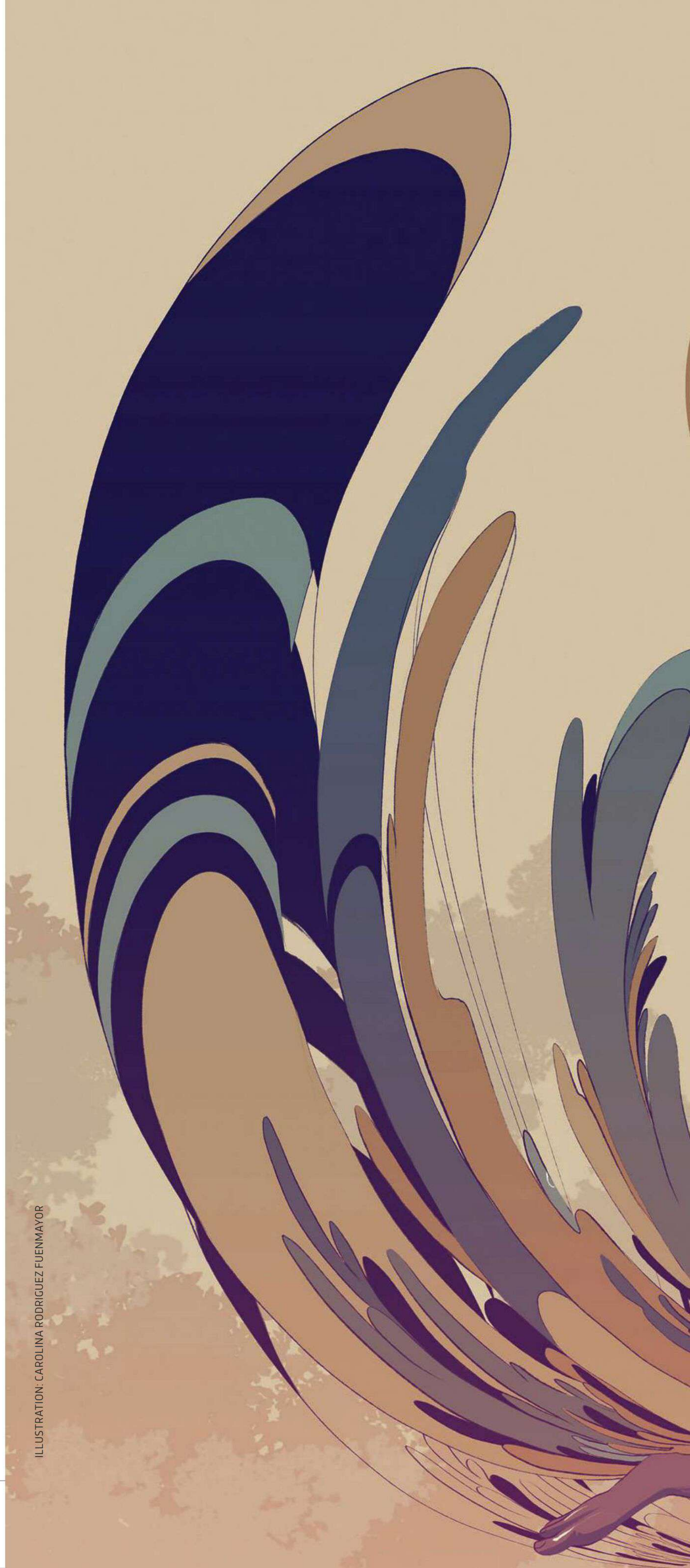


ILLUSTRATION: CAROLINA RODRIGUEZ FUENMAYOR

Alexander's story contains several features of what researchers today call a 'near-death experience' (NDE). The term was coined by the US psychologist and philosopher Raymond Moody in his 1976 bestselling book *Life After Life* in which he presented the accounts of 150 people who'd come close to death, noting that they often contained the same features, such as: a bright light; an out-of-body experience; the comforting presence of other people; feelings of wellbeing and reduced fear. It's possible to trace similar depictions further back in time, however. For instance, *Ascent of the Blessed*, painted by Hieronymus Bosch early in the 16th Century, features a bright light at the end of a tunnel.

Just as Alexander's story split opinion, so too have NDEs more generally. Some scientists, such as Dr Bruce Greyson, professor emeritus of psychiatry and neurobehavioural sciences at the University of Virginia and co-author of *The Handbook Of Near-Death Experiences*, believe that they challenge a purely physical account of human experience. NDEs "...present us with data that are difficult to explain by current physiological or psychological models," he wrote in 2013.

However, many others, such as Dr Charlotte Martial at the Coma Science Group at the University Hospital of Liege, and Chris Timmermann at the Imperial College Psychedelic Research Group, believe there *is* a scientific, neurochemical explanation for NDEs. Martial says she is "very convinced" by such explanations, though Timmermann cautions that "definite proof might be impossible with our current tools, because it would require for researchers to probe in the brains of human beings at the moment of death, which is unethical."

DRUGS AND NEAR-DEATH

The neurochemical account is given weight by a curious observation. Many of the key features of an NDE are recounted not only by people who have nearly died, but also by people who have taken psychedelic drugs. These include, but are not restricted to, psychedelics that act on the serotonergic system in the brain (serotonin is a neurotransmitter that's involved in mood and perception, among other functions). Such drugs are

"The parallels between psychedelic trips and near-death experiences have been observed for decades"

LEFT The painting *Ascent Of The Blessed* depicts a bright light and the presence of other people – similar to accounts of near-death experiences

RIGHT A shaman in the Amazon pours ayahuasca brew in readiness for a spiritual ceremony

ALAMY X2

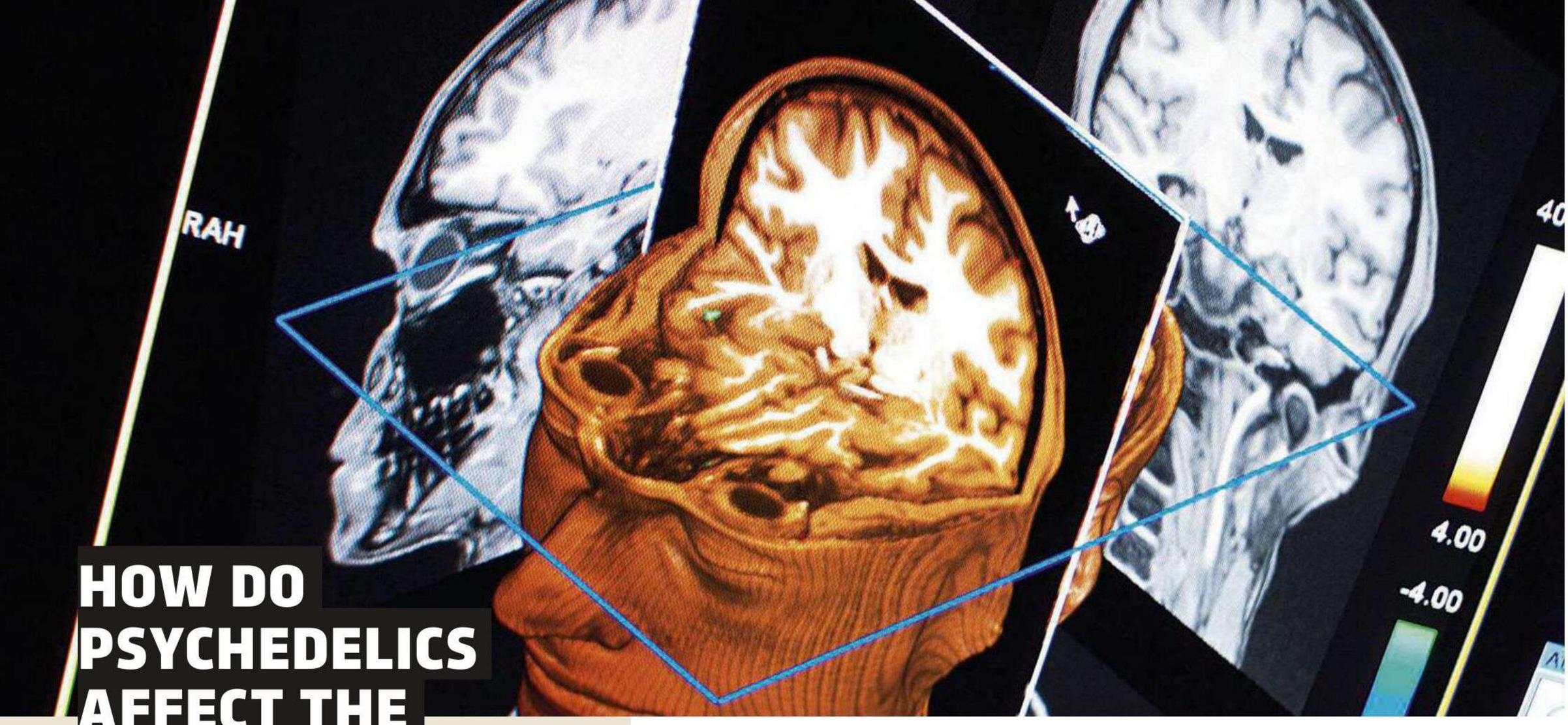
known as the 'classic psychedelics', and include LSD (lysergic acid diethylamide), psilocybin (the hallucinogenic compound in magic mushrooms) and DMT (dimethyltryptamine or 'spirit molecule', which is found in several plants located in the Amazon basin).

Psychedelic compounds have been used throughout history for spiritual adventure or to visit the afterlife. In the 16th Century, the Spanish Franciscan friar and missionary Bernardino de Sahagún described the use of mushrooms by indigenous people in Mexico leading them to experience "terrifying and amusing visions" and how "some saw themselves dying in a vision and wept". Further south, in traditional ayahuasca ceremonies in the Amazon rainforest, shamans still use a brew made out of DMT-containing *Banisteriopsis caapi* vine (they call it the 'vine of the dead') to contact spirits. In traditional cultures in central Africa, meanwhile, the psychedelic shrub iboga is used to induce an NDE as part of initiation ceremonies designed to broaden young people's minds.

Indeed, the parallels between psychedelic trips and NDEs have been observed for decades. It's notable that the second LSD trip ever experienced by a human featured classic NDE elements, as recorded first-hand by the discoverer of the compound, the Swiss chemist Albert Hofmann on 19 April 1943. "My body seemed to be without sensation, lifeless, strange. Was I dying? Was this the transition? At times I believed myself to be outside my body, and then perceived clearly, as an outside observer, the complete tragedy of my situation," Hofmann wrote in his book *LSD, My Problem Child*. Elsewhere, the controversial former Harvard psychologist and psychedelic evangelist Timothy Leary even likened to trips to "experiments in voluntary death". Yet it is only very recently that scientists have begun to make a formal comparison, opening the possibility of using psychedelics to model the experience of near-death. "One can hypothesise that some endogenous molecules [ones that are generated by the human body] mimicking DMT or ketamine mechanisms could be released in life-threatening situations, when an individual experiences an NDE," says Martial.

DELVING DEEPER

In 2018 an international team led by Timmermann and Robin Carhart-Harris at Imperial College, and including Martial in Belgium, conducted a small trial in which they asked 13 volunteers to complete a well-established measure of near-death experiences, both after taking DMT and after taking a placebo pill (for example, they rated how much they felt separated from their body, how much they had a sense of peace, and whether they saw a bright light). The researchers also compared their volunteers' experience under the influence of DMT with the reports of 13 people who'd had a 'real' NDE after a life-threatening episode. They found that, after taking



HOW DO PSYCHEDELICS AFFECT THE BRAIN?

'Classic psychedelics' like LSD and psilocybin (found in magic mushrooms) are chemically similar to the neurotransmitter serotonin produced by the brain. Serotonin is involved in many neural functions including mood and perception. By mimicking this chemical's effects, the drugs exert their profound effects on subjective experience. DMT too acts via serotonergic pathways, but also through other routes – for instance, DMT binds with sigma-1 receptors that are involved in the communication between neurons. Meanwhile, ketamine – among many other effects – blocks NDMA receptors that are involved in the functioning of the neurotransmitter glutamate.

A key brain area for psychedelic drugs' effects appears to be the temporal lobe, the location of much emotional and memory functioning. For instance, removal of the front part of the temporal lobe (as a radical treatment for epilepsy) has been shown to prevent the psychological effects of taking LSD. Interestingly, abnormal activity in the temporal lobe, such as during seizures, can lead to trip-like and NDE-like experiences.

An effect shared by different psychedelic substances is that they increase the amount of disorganised activity across the brain – a state that neuroscientists describe as being 'higher in entropy'. One consequence of this is a reduction in the activation of a group of brain structures known collectively as the 'default mode network', which is associated with self-conscious and self-focused thought. One theory, then, is that psychedelics provoke a spiritual state of oneness with the world by increasing the brain's entropy and suppressing the ego-sustaining activity of the default mode network.

DMT, all 13 of their volunteers had effectively had an NDE based on their scores on the formal near-death questionnaire. The team also observed "few discernible differences" between the actual NDE cases and those induced by DMT. In a study published in March 2019, Martial led another international research group who took a different approach to the same question. They compared the similarity of the first-person descriptions of approximately 15,000 psychedelic trips with the retrospective first-person accounts of several hundred near-death experiences collected in Belgium and the USA. The similarities between the two kinds of experience were striking, with the NDE-like nature of the trips being especially apparent for people who'd taken one of the classic psychedelics, and most of all for people who'd taken ketamine – a so-called 'dissociative psychedelic' that is used in medicine as an anaesthetic. "In short, researchers now have indirect and more direct empirical evidence of certain neurophysiological mechanisms underlying NDEs," says Martial.

DEFINING DEATH

There are also similarities in the long-term effects of NDEs and many psychedelic trips. In both cases, people who have been through the experiences describe them as feeling 'realer than real', highly memorable and personally transformative. For example, a 2019 study involving dozens of people who'd had an NDE found that more than half considered it a self-defining memory. Similarly, psychedelic experiences have been shown to have lasting effects on personality, with people frequently describing their trip as one of, if not the most personally meaningful and spiritual events of their lives.

Martial and other researchers believe that the reason that many psychedelic trips are subjectively and psychologically so similar to NDEs is that, close to death, the brain releases chemicals that are the same as, or act in a similar way to, psychedelic compounds. Supporting this neurochemical account, DMT is known to be present in the brains of humans and other mammals, and a study published in the summer of 2019 even found that concentrations of DMT increased after cardiac arrest was induced in rats – perhaps as a function of its neuroprotective properties. Other scholars have made a

RIGHT The academic Timothy Leary likened drug trips to "experiments in voluntary death"

proposal that a ketamine-like substance with a similar protective function might be released close to death.

There are also similarities in the level of changes seen in brain activity observed after cardiac arrest and following ingestion of psychedelics – in both cases, activity becomes more synchronised across the entire brain. It is speculated that this might be responsible for feelings of oneness with the world, also known as 'ego dissolution'.

"A ketamine-like substance with a protective function might be released close to death"

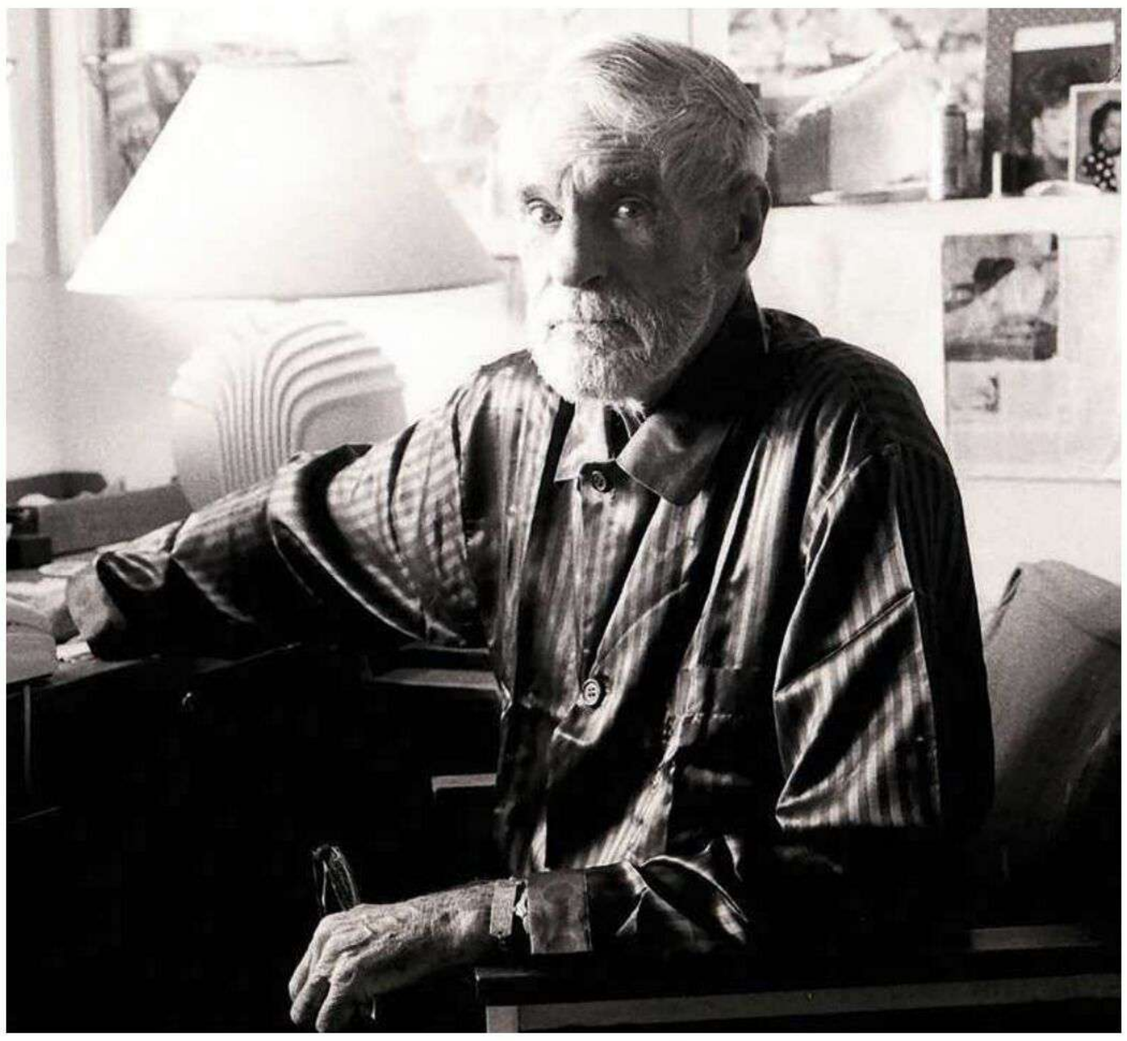
Not everyone is entirely convinced by the current proposed neurochemical explanations. For instance, the US pharmacologist and international psychedelics expert Prof David Nichols wrote a paper in 2018 in which he argued that the concentrations of DMT in the brain are too minute to be responsible for the psychoactive effects observed during NDEs. However, he says that "as a scientist, I do believe there is a neurochemical explanation for an NDE."

Timmermann, who led the aforementioned 2018 comparison of DMT trips and NDEs, hears Nichols's concerns but still believes that endogenous DMT may play a role in NDEs, possibly alongside other neurochemicals. And even if it turns out that chemicals such as DMT or ketamine are not involved in NDEs, he argues that psychedelics provide a useful model for studying the psychological experience of dying. "…[T]he experience of death is something which we are only beginning to become interested in from a scientific perspective, and thus models which can be safely used in controlled environments will be valuable for us to understand what these experiences are about and also why they might have such a strong impact on people's lives," he says.

The experience of death is still largely unchartered territory for science, and for obvious reasons (Martial and her colleagues noted wryly in their 2019 paper that "…dying is difficult to study under controlled laboratory conditions by means of repeated measurement"). Even if NDEs provide a window into the experience – and psychedelics can be used to model and investigate the same or similar processes – it's notable that the majority of people who are resuscitated after being close to death do not report NDE-type memories of what happened. "Since no one has actually died and come back to tell about it – I mean a death that is not reversed – we can't know whether DMT or ketamine are good models," says Nichols bluntly. "They may model the NDE, but we don't know whether an NDE is actually similar to the experience of dying."

On a positive note, the profound, NDE-like nature of many psychedelic trips has opened new avenues for helping alleviate existential suffering for people with terminal illnesses. Just as many people who emerge from classic NDEs subsequently report a dramatic loss of fear for the afterlife, so too do individuals who have enrolled in trials for psychedelic-assisted therapy for existential anxiety. Research groups around the world are now exploring these therapeutic possibilities, including at New York University, Imperial College in London and at the just-opened Center For Psychedelic Research at Johns Hopkins Medicine in the USA.

Could there be a risk that psychedelic research, by explaining NDEs in biochemical, rather than spiritual terms, will undermine the hope and relief that many people find in stories of NDEs? If the sensations of bliss, light and love come from neuroprotective molecules rather than being 'proof of heaven', is this an area of research best left alone? Like many working in this field, Dr Frederick Barrett at Johns Hopkins thinks not. "I generally disagree with the premise that explaining the biochemical basis of something undermines the subjective experience, meaning, beauty, terror, or otherwise the value of an experience," he says. "Does explaining the physics of centripetal acceleration make a rollercoaster any less exciting or terrifying? Not for me, and I would imagine: not for most." **SF**



MARTIN HIESLMAIR, GETTY IMAGES

by **DR CHRISTIAN JARRETT** *(@Psych_Writer)*

Christian is a senior editor at Aeon *magazine. His next book, on personality change, will be published by Simon and Schuster in early 2021.*

ARE YOU READY TO USE COMPUTERS TO BOOST YOUR BRAIN?

Mind-machine interfaces have the potential to upgrade our intelligence and supercharge our thinking. But at what cost?

by LUCY MADDOX

Would you have an IQ-boosting microchip implanted in your brain if you had the chance? What if everyone else around you did? Imagine your work colleagues outperforming you, and your friends having conversations you can't quite follow. Would you upgrade your brain then? Should you?

It sounds like science fiction, but it's not such an outlandish idea. In 2019, an announcement from tech entrepreneur Elon Musk's company Neuralink caught the attention of the world's media. A range of different ways to link brain signals and computers – brain-computer interfaces, or BCIs – already exist, but Neuralink has improved this technology using impressively small, super-thin, flexible micro-electrodes, which enable a tiny device to be implanted in the brain to read (and potentially write) neural signals. They have trialled this in monkeys, and seek to trial it in humans.

So far, research has focused on the many possible medical applications for BCIs, but Neuralink also wants to create a device that can be used by healthy people for brain improvement. Cognitive enhancement could be the future Botox. But although a tuned-up brain could expand human possibilities, some experts are already cautioning of the dangers that may lie ahead. Brain enhancement of healthy individuals is not yet possible, but Dr Davide Valeriani is one expert who thinks that it could become an option within his lifetime.

"All big companies are interested in jumping into brain-computer interfaces," explains Valeriani, a postdoctoral researcher in BCIs at Harvard Medical School in the US. He lists Amazon, Facebook and Microsoft, as well as agencies such as the US military. "If big companies work on this then we can push the research. They have more resources."

MIND MACHINES

As well as the technical challenges associated with implanting a chip in the brain, Valeriani points out that there are other, more intangible problems to solve. The benefits of BCIs in helping individuals who are paralysed or brain-damaged are clear to see, but the advantages for healthy individuals would have to be extra special to outweigh the risks of the invasive surgery, and overcome a range of ethical dilemmas. Potential problems include the possibility of 'brain-hacking' (a person or agency somehow taking control of the chip or accessing data), and ethical compromises if the technology is used experimentally in countries with a poor human rights record. In addition, the animal experiments needed to develop the technology are one thing when viewed in the context of helping paraplegia, and quite another when viewed in the context of souping up the brain.

So what are the potential benefits? Why would we want electrodes implanted in our brains? Valeriani is working on improving decision-making, especially decisions that might have a large negative impact

ILLUSTRATION: ANDY POTTS

ALAMY X2, SCIENCE PHOTO LIBRARY, RICK FRIEDMAN, URMIL, GETTY IMAGES

BRAIN COMPUTER INTERFACES: THE SCIENCE SO FAR AND THE TECHNOLOGY TO BRAVE

ABOVE
Brain-computer interfaces have come a long way, but they're still some way off becoming unobtrusive

if we get them wrong, for example a doctor misdiagnosing a medical problem, or a soldier making a bad choice in a military situation.

"What I see as the advantage of BCIs is that you keep the human in the loop," says Valeriani. Rather than handing over all our decision-making to artificial intelligence (AI), BCIs could assist us with our dilemmas, helping to modulate and correct our inherent biases and blind spots. "If a human is assisted by a BCI and then there is another completely independent machine that makes a decision based on the same information, you can merge the two decisions together, and we showed recently that they work better together than each of them alone," says Valeriani.

Research is also advancing BCI-assisted communication. "BCIs are not reading thoughts," says Valeriani, "they're looking for patterns." Computers can be trained to recognise patterns of brain activity that occur when, for example, we're thinking about a certain object, or willing a particular body part to move. It's this technology that allows people to move prosthetic limbs with their thoughts. Getting better at this pattern recognition might eventually allow us to identify the specific contents of people's thoughts, therefore opening up a whole world of possibilities such as telepathic communication, being able to update our Facebook statuses with our minds, or drive our cars by thought. We're far from the required resolution yet, but the potential is there.

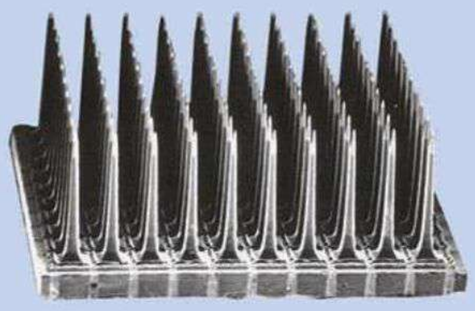
Another possibility is computer-based memory extension. We already treat our computers and smartphones as a kind of memory aid, using them to store our work, photos, calendars and conversations. What if BCIs could one day increase the amount of memory that is instantly available to our

1973

The first brain-computer interface (BCI) is created by Jacques Vidal (below) at the University of California. He uses non-invasive electroencephalogram (EEG) recordings of brain activity to communicate with a computer.

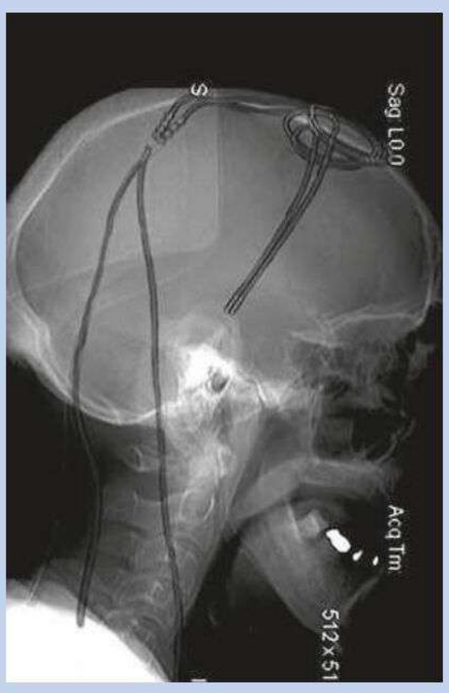
1988

Researchers in the former Yugoslavia use EEG brain signals to control a physical object for the first time – issuing commands to a robot by simply opening and shutting their eyes.



1991

A 100-electrode device called the Utah Array (above) is invented by Richard A Normann. It can be implanted in the brain to stimulate brain cells, or to record their output to electronic circuitry.



1997

Deep brain stimulation, which involves implanting electrodes into the brain (above), is approved by the US Food and Drug Administration for the treatment of the tremors of Parkinson's disease.

2000

Researchers at Duke University, North Carolina, develop a BCI that can decode brain activity in monkeys and reproduce the monkeys' arm movements in a robot.

2005

Matthew Nagle (below) becomes the first person to control an artificial hand using thought. Paralysed from the neck down, Nagle also uses the brain-reading technology – developed by Massachusetts-based company Cyberkinetics – to play games, operate a TV and access emails.

2016

Another paralysed man, Nathan Copeland (above), is the first to be given a sense of touch through a mind-controlled robotic arm, thanks to a BCI developed at the University of Pittsburgh that stimulates the sensory region of the brain.

2019

Elon Musk (above) unveils Neuralink's plans for its advanced BCI technology, which involves using a specially built surgical robot to insert thousands of flexible, thread-like electrodes into the brain.

HOW IT WORKS:
NEURALINK

The tech behind Elon Musk's brain-reading machine

1. Each of Neuralink's new 'n1' sensors fits into a case measuring 8mm in diameter and 4mm in height.

2. All of the components of the Neuralink are stacked inside the case and hermetically sealed.

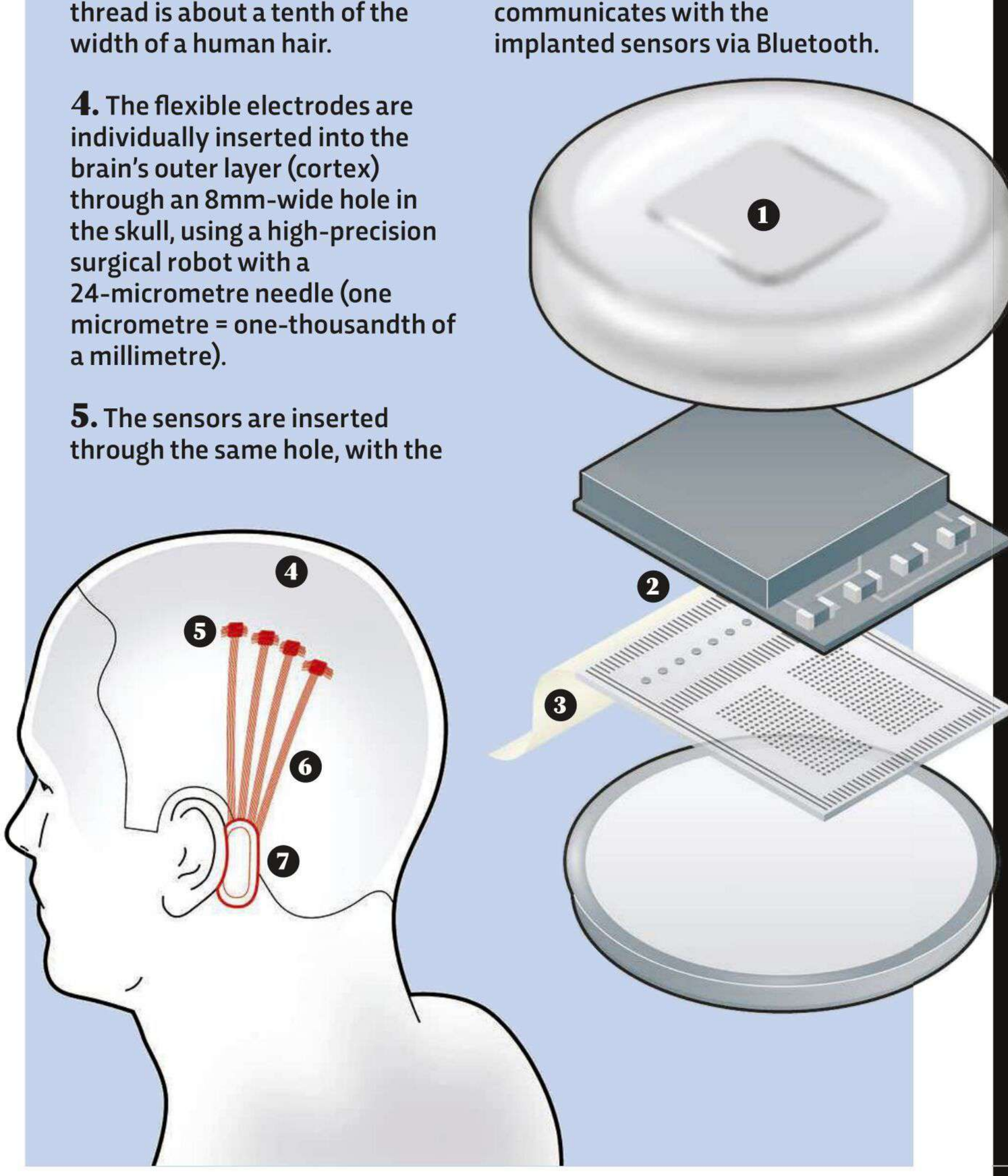
3. Each sensor is connected to 1,024 flexible, thread-like electrodes capable of reading and writing to nerve cells (neurons) in the brain. Each thread is about a tenth of the width of a human hair.

4. The flexible electrodes are individually inserted into the brain's outer layer (cortex) through an 8mm-wide hole in the skull, using a high-precision surgical robot with a 24-micrometre needle (one micrometre = one-thousandth of a millimetre).

5. The sensors are inserted through the same hole, with the skin being closed up over them. Up to 10 sensors could be implanted, meaning as many as 10,000 electrodes.

6. The sensors are connected to an induction coil beneath the skin behind the ear, via thin wires tunnelled under the scalp.

7. The induction coil connects through the skin to a wearable device called 'The Link', which sits behind the ear and communicates with the implanted sensors via Bluetooth.



brain, allowing us to store memories of everything we've ever experienced, and never forget a face or a name?

Last year, researchers led by Dr Robert Hampson at the Wake Forest School of Medicine, North Carolina, successfully improved people's short-term memory by directly stimulating brain cells in their hippocampus – an area of the brain involved in memory. The scientists recorded the pattern of brain cell activity during remembering, and then used the same pattern to stimulate the cells while a memory task was being carried out – increasing performance by over 35 per cent. The participants in this experiment were epilepsy patients who were already having electrodes implanted in order to monitor their seizures, but the scientists are hoping to develop this technology to help with dementia, and it may one day find its way into BCIs for healthy individuals, too.

Although the technology isn't there yet, Valeriani thinks that a removable device would be a better option for healthy individuals, so that it could be kept outside the body and switched off when necessary. "So if we don't want to use it, we don't have to... we'd be able to separate 'what is me' from 'what is technology'."

IDENTITY CRISIS

The question 'what is me?' takes BCIs into the realm of philosophy. Dr Susan Schneider, a philosopher and cognitive scientist at the University of Connecticut, is interested in the links between future technology, the mind and the self.

"Imagine walking into a mind-design centre of the future, like a cosmetic neurology centre, and seeing a menu in front of you with all these enhancements," she says. She imagines being able to reach the meditative states of a Zen master, or gain the musical abilities of Mozart – or even sculpt your personality.

"I understand the pull of all of this," says Schneider. "But if you decide you're going to purchase a bunch of these

NEUROLINK ILLUSTRATION: ACUTE GRAPHICS

"If you purchase a bunch of these enhancements ... is the person who emerges truly you?"

enhancements… is the person who emerges truly you?" She thinks there will come a point when a person replaces so much of their brain with artificial components that they've actually killed themselves without realising it.

This riffs on classic thought experiments. How much of our brain do we need to keep in order to be the same person? If we suddenly lose our memories, does this mean we're not us? What about if a brain injury affects our personality? What makes me 'me'?

THINKING AHEAD

University of Sussex neuroscientist Prof Anil Seth likes to think about the potential problems around BCIs in terms of a 'worry budget'. As we only have so much worry to go round, he argues, we should spend it on more immediate concerns related to our use of technology, such as social media algorithms, which influence what we see online and therefore our behaviour. In the realm of decision-making, he thinks we need to consider, now, who will be responsible if future AI helps us to make a bad decision.

He's not so worried about AI becoming conscious, or accidentally modifying ourselves out of existence. "I'm not sure I'd worry too much specifically about no longer being the same person," he says. "We are always changing who we are, even if we do not perceive this."

Seth is also concerned about equality. "We can get caught up in the technological and scientific excitement, but equality of access is important. We could start to see people who are developing and purchasing this stuff pull apart from the rest of the population. That's something that ought to keep people up at night."

Whatever we choose to spend our personal worry budgets on, BCI technology is advancing fast. Some transhumanists (who think technology should be used to enhance the human condition) have already implanted microchips in their bodies to act as door keys or credit cards. The technology to implant microchips in the brain, or perhaps a non-invasive, removable alternative, is not inconceivably far away.

Whatever happens next, Valeriani, Schneider and Seth agree that we need to keep the ethical and philosophical dilemmas in mind as the technology evolves. The answer to whether we should upgrade our brain relates to bigger 'shoulds' about fairness, responsibility and who we consider ourselves to be. Perhaps it also relates to what sort of people we *want* to be. Is it enough to want to be upgraded? Or should we be upgrading our social and ethical ambitions instead? **SF**

by **DR LUCY MADDOX**
(@lucy_maddox)
Lucy is a consultant clinical psychologist who writes about psychology and neuroscience.

IS ANYBODY IN THERE?

by AMY FLEMING

Groundbreaking new research has discovered that 15 per cent of coma patients might be conscious and aware of their surroundings. Now, the race is on to find out ways to bring them back...

The rare occasions when people in vegetative states 'wake up' after years or even decades of unresponsiveness always make the news. We're fascinated by the details behind the jubilant headlines: what was it like waking up from an extremely long sleep? What had been going on in their minds? Were they frozen in time? Or had they, perhaps, been aware of what was going on around them the whole time?

It's hard to gauge how many people are currently in a persistent vegetative state, languishing in a care-home bed, their inner lives a mystery. The causes of their brain injuries are diverse – from oxygen starvation (which could be due to stroke, heart attack, near-drowning and more) to trauma caused by a blow to the head – and there is no central register. But neuroscientists estimate there are thousands in the UK, and they are increasing in number, as doctors get better at saving lives in the aftermath of brain injuries.

Thankfully, doctors are also getting better at figuring out what is going on in these patients' minds. "There have been huge discoveries over the last 15 years," says Prof Adrian Owen, from the Brain And Mind Institute at Canada's Western University. The first of these, he says, was "a 2006 paper where we showed that some of these patients are actually aware, and then the 2010 paper where we started to communicate with some of them."

From the data so far, 15 to 20 per cent of patients show signs of concealed consciousness, and researchers are now making great strides in diagnosing the condition, understanding its mechanics and even working on treatments that could increase the chances of rehabilitation.

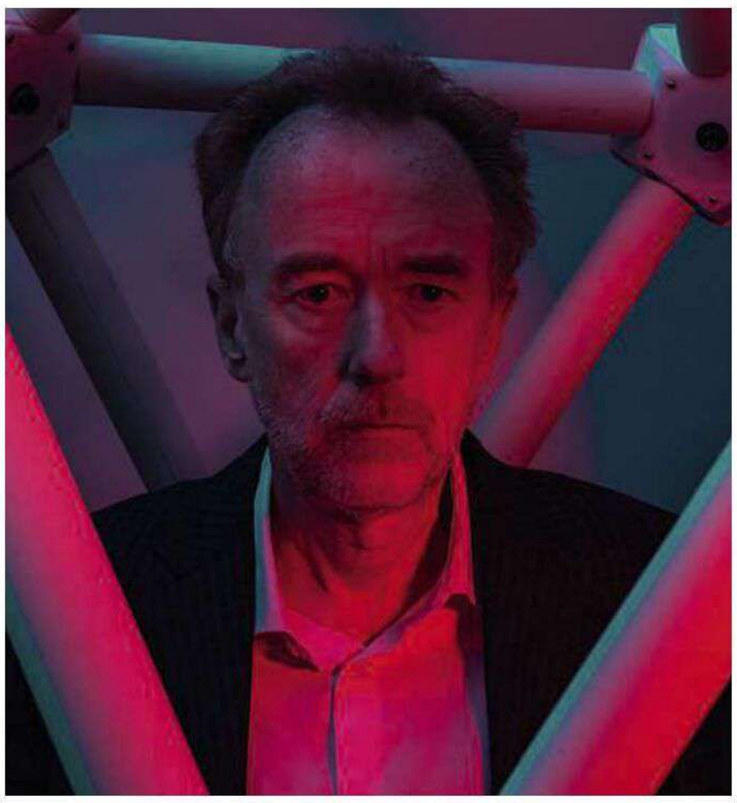
INTO THE UNKNOWN

Technically speaking, coma usually only lasts for days or weeks after an injury. "Typically, you don't go through the screen of a car and straight into a vegetative state," says Owen. "First, your eyes are closed and you're on life support." This is a coma – an acute disorder of consciousness. It's only after a patient emerges from the coma that they either wake up, are diagnosed with brain death (for which there are clear metrics), or enter a prolonged disorder of consciousness.

"This may be a vegetative state, or what we call a minimally conscious state, or MCS," says Dr Davinia Fernández-Espejo, a senior lecturer at the University of Birmingham, whose study earlier this year identified the physiological cause of vegetative state, and who is developing a therapy to treat it.

In a vegetative state, the patient is off life support, able to breathe on their own and digest food. "They often appear to be awake," says Fernández-Espejo.

ILLUSTRATION: SÉBASTIEN THIBAULT



LEFT Adrian Owen from Canada's Western University led the team who first began talking to patients who were otherwise deemed unresponsive

"Their eyes are open and moving around a little bit." They might startle if you blast some Led Zeppelin, or withdraw their hand if you poke them, she explains, "but they still don't respond to the environment in any intentional way that may make us think that the patient is aware."

Minimally conscious people show flickers of awareness, but "they're still incapable of communicating – verbally or non-verbally."

DETECTING CONSCIOUSNESS

So how can doctors tell if there is concealed consciousness? Owen has developed a method using an fMRI scanner. He asks a series of questions: to answer 'Yes', the patient imagines they're playing tennis, while to answer 'No' they take a mental stroll around their home. If they're conscious, different areas in the brain will light up: motor activity for 'Yes' versus spatial awareness for 'No'.

It's in intensive care units (ICU) where doctors and families often have to decide whether a patient has prospects for survival or whether life support should be turned off – and mistakes will have inevitably been made. But now, says Owen, "we can apply these techniques in the ICU, maybe a week after their injury, and both diagnose them more accurately and make predictions about who's going to recover and who isn't."

However, fMRI scanners can't simply be wheeled into an ICU. So, in a small 2019 study, Columbia University-based neurologist Jan Claassen showed that an electroencephalogram (EEG) that measures brain waves, combined with machine learning, could be used instead to detect concealed consciousness in ICU patients. Once again, the patients were asked questions and their brain activity was observed. Within four days of their injuries, 15 per cent of the 104 patients in the study were found to have hidden consciousness, despite being unresponsive.

Of those patients, 44 per cent progressed out of their vegetative state, to some degree, within 12 months.

Owen, meanwhile, has developed a new portable technique, "based on a method called functional near-infrared spectroscopy, which like fMRI looks at the amount of oxygen in the blood, only with little lasers. It's pretty cool. We had a paper out last year showing that we could use it effectively to communicate with a patient," says Owen. The team asked the patient if he felt safe and if he was in any pain. "He wasn't," says Owen, "and he felt at peace with himself as much as one could."

One of Owen's Canadian patients, Juan Torres, had an acute brain injury after choking on vomit, but made an unprecedented recovery to the extent that he could clearly recount his three-month vegetative experience. He'd witnessed doctors declaring his brain irreparably damaged, and his family's devastation. "He said he was always trying to move but it just wouldn't happen," says Owen.

It's not that vegetative patients are paralysed – that's a different condition called locked-in syndrome, where there is obvious consciousness but the connection between the brain and spinal cord is severed. Fernández-Espejo's research group has discovered that vegetative patients with covert consciousness have "damage in some fibres connecting the thalamus in the centre of the brain, and the motor cortex, which controls movement. Because this pathway is injured, these patients are not able to voluntarily control their behaviour."

Many of these patients will have severe damage to other parts of their brains, too, "but the damage to other cognitive functions is not as severe as it looks from the outside, because of these problems with controlling the movement," says Fernández-Espejo.

Her group is now recruiting patients to trial a non-invasive form of electrical stimulation. The hope is that this will encourage "the neurons that are still there to work harder to compensate for the

"AN EEG, COMBINED WITH MACHINE LEARNING, COULD BE USED TO DETECT CONCEALED CONSCIOUSNESS"

ones that were lost, so the patient can make some small movements." This could then enable patients to use technology to communicate, in the way many locked-in people can, and get them to a point at which rehabilitation therapies are possible.

"I'm really excited to be at this stage," says Fernández-Espejo, "after years of being been able to say to relatives, 'Yes, the patient is conscious,' but then not being able to do anything about it. Now we have a mechanism that we can exploit to try to help patients get better."

A NEW HOPE

Dr Theresa Bender Pape, a clinical neuroscientist with the US Department of Veterans Affairs based at Northwestern University in Chicago, is currently trialling another non-invasive treatment called transcranial magnetic stimulation (TMS) to alter brain activity in vegetative patients. The results are due for publication in 2020, and are promising. The idea is, she says, "I get one neuron to talk to the next neuron to talk to the next neuron, so I'm altering neural activity in areas remote from the site of stimulation over time."

Pape has also developed a treatment called Familiar Auditory Sensory Training (FAST). It involves close relatives recording well-worn family stories and jokes, and these recordings being played to the patient repeatedly. In 2015, a placebo-controlled study assessing FAST's impact showed that patients who received the therapy recovered sooner and more extensively than those that didn't. And in answer to relatives wanting to know whether their loved ones could hear them, MRI scans showed patients' brains lighting up in response to the stories, in regions associated with language and long-term memory. "I love when patients tell me that they remember the stories," says Pape.

Pape's star TMS recoverer, Laura Gonzalez, is now sitting up, communicating non-verbally and living back at home, after more than 18 months in a vegetative state. After around 20 TMS treatments (out of 30), she recalls, "I walked in the room and said, 'Hey Laura!'" When Laura looked back in acknowledgement, she says, "I thought: 'Did I just see that?' The hair on the back of my neck stood up." **SF**

DISCOVER MORE

BBC RADIO 4 *Listen to Adrian Owen tell Jim Al-Khalili about his research on people in comas in this episode of* The Life Scientific
bit.ly/Adrian_owen

by **AMY FLEMING** *(@Amy_Fleming)*
Amy is a freelance science journalist whose work has appeared in The Guardian, Newsweek *and the* Financial Times.

SCOTT HEINS, ILLUSTRATION: SÉBASTIEN THIBAULT

THE BITE THAT CURES

The evolutionary arms race between prey and predator has created some of the most deadly molecules on Earth. Now, scientists are repurposing these venoms to create the next generation of wonder drugs

by KATH NIGHTINGALE

ZOLTAN TAKACS

Around 150,000 animal species have evolved the ability to produce venom. And, as Dr Zoltan Takacs says, it's evolution that has turned this venom into a such strong source of medicine

To most of us, medicine comes from the chemist. There we can stock up on blister packs of pills, tubes of ointments and bottles of innocuous-looking liquid. But the original sources of drugs can be much more exotic than your local pharmacist. The first HIV drug, for example, came from a sea sponge, while a heart disease drug is derived from the foxglove plant.

You can't get much more exotic than venomous animals and that's where scientists are turning their attention. Venoms are cocktails made up of between tens and hundreds of different toxins, usually proteins and smaller chains of amino acids similar to proteins called peptides, along with organic molecules, such as hormones, antibiotics and other compounds that are involved in the metabolic functions of living things. Venoms help animals to immobilise or kill prey, or neutralise predators in self-defence.

To qualify as venom, as opposed to poison, the toxin mixture must be 'injected' into another animal. Around 150,000 animal species have evolved the machinery to produce venom and inject it into prey. Some are familiar: snakes with their fangs, or bees and their stings. Others are less well known: the male duck-billed platypus with the venom-bearing spurs on its back legs; the toxic saliva of particular types of shrew; the beautiful but deadly cone snail releasing its harpoon-like proboscis into tiny fish on the seabed...

It's evolution that's made venom such a good source of drugs, says Dr Zoltan Takacs, a Hungarian-born scientist-adventurer who founded the World Toxin Bank. "Venom toxins are among the most potent and precision-targeted molecules on Earth," he explains. "From mankind's point of view, this makes venom toxins ideal templates for drug discovery."

Over hundreds of millions of years, the toxins in venoms have been honed to target highly specific components of their prey's vital bodily functions. Some toxins attack the nervous system, causing paralysis by interfering with nerve-to-muscle communication. Others prevent blood clotting, resulting in massive bleeding. Yet it's these same dangerous properties that could make them useful. Substances that interfere with the nervous system could make great painkillers, while blood thinning is a vital part of treatment for heart disease.

"It almost gives you the luxury of tweaking some of the best pieces of molecules that evolution designed"

Dr Zoltan Takacs' work in animal venom led him to establish the World Toxin Bank

DON'T TRY THIS AT HOME

But this doesn't mean that doctors will soon be recommending you keep a few venomous snakes and spiders around the house. "Venom is a complex mixture of toxins," says Takacs. "You need to isolate a single particular toxin to have a safe therapeutic agent."

Using venoms as a source of drugs isn't a new idea. Ancient civilisations used venoms in medicines, and the first venom-derived drug of modern times became available in the UK in 1981. There are now around 20 different medications originating from animal venoms, says Takacs, targeting everything from heart disease to diabetes.

But only recently have scientists been in possession of the technology necessary to systematically search through venoms for likely drug candidates. Takacs collects venoms from around the world, often in remote areas, to get his hands on new venom samples.

Using Designer Toxins technology, which he co-invented, Takacs fuses natural toxins from different venomous animals into a single molecule. This technique is used to create vast libraries of toxin variants, such as the World Toxin Bank, that can be screened against known drug targets to find toxins that have the highest promise to treat diseases.

"Imagine fusing pieces of snake, scorpion and sea snail toxins together and ending up with variants that are rooted in nature, yet have new biological properties," says Takacs. "It almost gives you the luxury of hand-picking and tweaking some of the best pieces of molecules that evolution ever designed."

With around 20 million venom toxins in nature left to explore, it looks like we may be seeing more and more drugs inspired by nature's powerful venoms in our bathroom cabinets. So where might they come from?

A patient allows his hand to be stung by a honeybee as part of a programme of bee venom therapy

The volume of venom found in a bee sting can be up to 25 times greater than a wasp sting

BEES AND WASPS

TARGETS: HIV, breast cancer, skin cancer and rheumatoid arthritis

Of all the venomous bites, stings and punctures, the ones most of us will be familiar with are those from bees. Bee venom, though, contains compounds that could have uses as diverse as combatting HIV and helping to treat rheumatoid arthritis. More than half of the venom of honeybees is made up of a peptide called melittin. Despite its diminutive size, this toxin packs a mean punch – it's the cause of the burning sensation that comes along with a sting. In lab tests carried out by researchers at Washington University School of Medicine in the US, gold nanoparticles carrying melittin can puncture holes in the protective envelope of HIV without affecting human cells. These nanoparticles could one day be part of a vaginal gel to prevent HIV transmission.

One of the biggest challenges facing cancer therapy is how to ensure that drugs target only cancerous cells and not healthy ones. Researchers from the University of Leeds and São Paulo State University in Brazil are studying a toxin from the venom of the Brazilian wasp *Polybia paulista* that could do just that. It targets structures of fatty molecules on the outside of cancer cells, puncturing holes in the cells and causing vital molecules to leak out. Those same fatty molecules are found on the *inside* of healthy cells, so non-cancerous cells are safe from the wasp toxin's attentions. The toxin has only been tested in the lab, so don't start welcoming wasps into your home just yet.

Melittin's puncturing properties could also be useful in cancer treatment. It's been shown to shrink tumours in mice with breast and skin cancers when delivered via nanoparticles. It can also block the inflammatory mechanisms in cells and animals with rheumatoid arthritis.

The toxin of the Brazilian wasp *Polybia paulista* is the ideal weapon against cancer since it leaves normal cells unharmed

SNAKES

TARGETS: Blood pressure, blood clotting and chronic pain

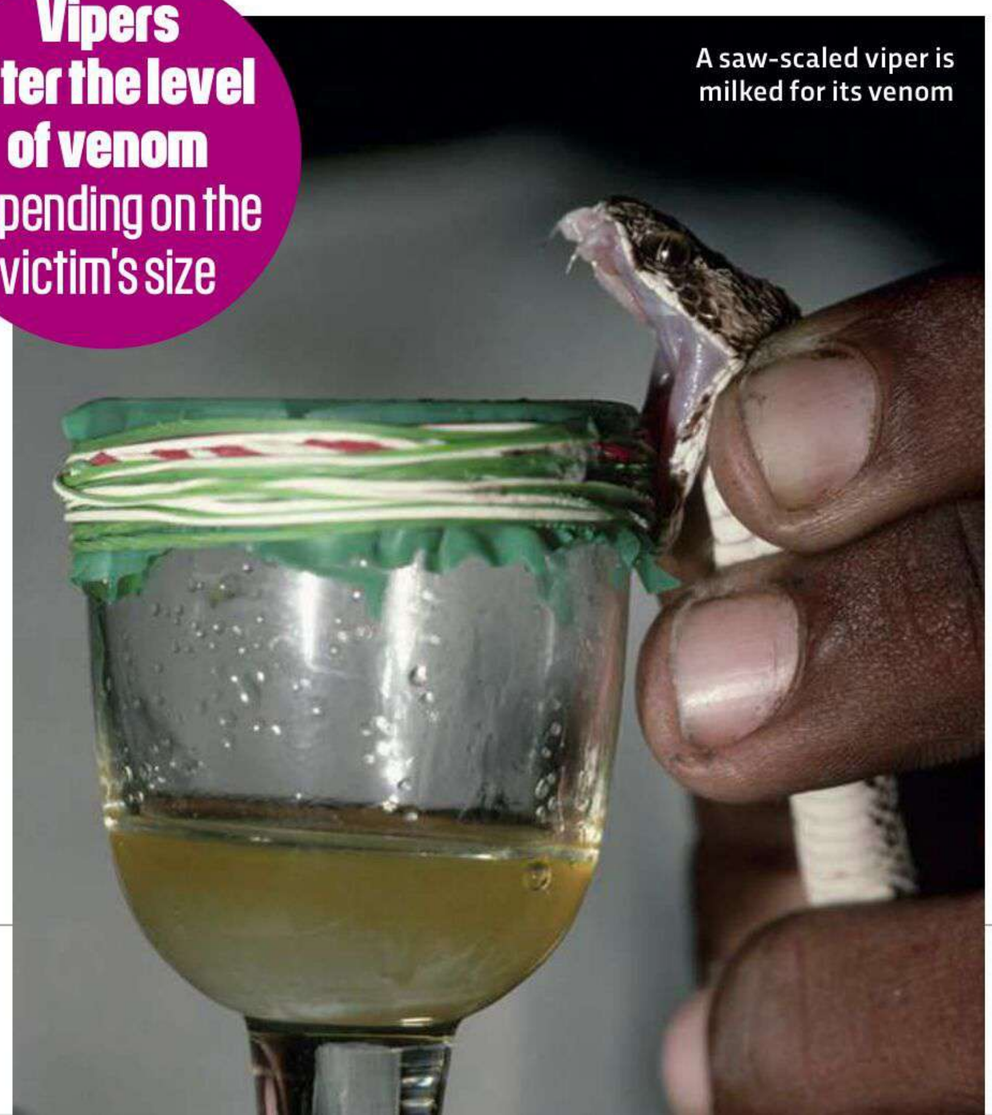
If you were asked to think of a venomous animal, it's fairly likely that a snake would be the first that springs to mind. They're also probably the most studied among scientists in search of new drugs.

Many snake-derived drugs target the cardiovascular system. Workers on banana plantations who've been bitten by snakes often pass out due to severe drops in blood pressure. This led researchers to a peptide in the venom of the pit viper *Bothrops jararaca*. The drug based on it – blood pressure medication captopril – works by stopping the molecules that would ordinarily prevent blood vessel dilation, allowing them to widen and lower blood pressure. It was the first venom-based drug and continues to be one of the most popular medications on the market.

The southeastern pygmy rattlesnake, found in the US, has potent venom that stops blood from clotting and causes profuse bleeding. One of its toxins has been developed into a drug called eptifibatide that is used in people who are at risk of having a sudden heart attack. It stops platelets in the blood from sticking together, preventing the blood clots that can cause heart attacks and strokes. A similar toxin, from the venom of the saw-scaled viper, has the same target and is the basis of the drug tirofiban.

A potential treatment for heart failure is cenderitide, which is made of a peptide from the eastern green mamba fused with another peptide from human blood vessel cells. And France's Institute of Molecular and Cellular Pharmacology is researching a toxin from the black mamba as a possible new painkiller, after studies in mice found it to be as powerful as morphine.

Vipers alter the level of venom depending on the victim's size



A saw-scaled viper is milked for its venom

GETTY IMAGES X2, ZOLTAN TAKACS

CONE SNAILS

TARGETS: Chronic pain, Alzheimer's, Parkinson's, schizophrenia and lung cancer

These predatory carnivorous sea snails are found mainly in the warm Indian and Pacific Oceans and their toxins are already proving useful as painkillers. Their 'bite' comes from a modified tooth that is projected out of the snail's mouth and injects venom into its prey, usually fish, instantly paralysing it. Once immobilised, the prey can be engulfed and digested by the snail.

While it's bad news for the fish, some of these same toxins have shown painkilling effects in humans. There is already a drug on the market – the morphine-like ziconotide – which is used to treat severe chronic pain by administering it direct into the spinal fluid. It is a synthetic copy of a peptide from the venom of *Conus magnus*, also known as the magical cone.

Another snail toxin is being investigated by the University of Utah for its ability to affect nicotinic receptors in the brain which, as well as being involved in tobacco addiction, can play a role in Alzheimer's disease, Parkinson's disease, schizophrenia and lung cancer. And with each cone snail species producing its own distinct venom, there are probably plenty more where they came from.

One species, *Conus geographus*, is known as the 'cigarette snail' because a human victim of its sting would only have **time to smoke a cigarette before they died**

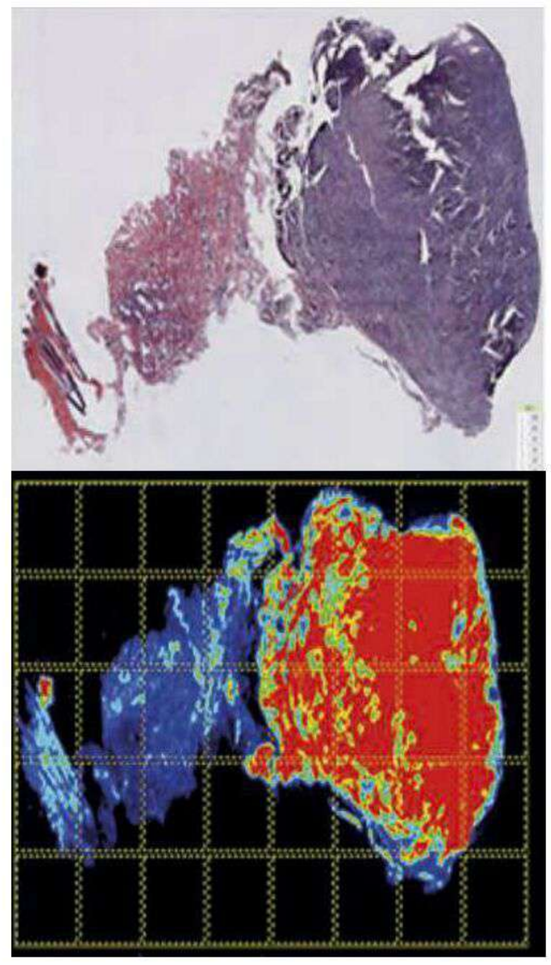
SPIDERS, SCORPIONS AND CENTIPEDES

TARGETS: Cancer, muscular dystrophy, chronic pain and erectile dysfunction

Scorpion venom could be medically useful as a way of marking up brain tumour cells for surgery, as it's tough for surgeons to identify where a tumour ends and healthy cells begin. If they err on the side of caution, cancer cells get left behind. If they get too knife-happy, then healthy cells are cut out alongside cancer. Chlorotoxin, a component of venom from the cheerily named deathstalker scorpion, binds to tumour cells. Adding a fluorescent tag means that tumours 'light up', allowing a surgeon to clearly see their boundaries. This 'tumour paint', developed by researchers at the Fred Hutchinson Cancer Research Center in the US, has been tested in animals and is now being trialled in people.

Spider venom also appears to be a rich source of compounds for drug development, with toxins believed to have the potential to variously treat muscular dystrophy, chronic pain and erectile dysfunction.

Staying with arthropods, studies by researchers from the University of Queensland in Australia and China's Kunming Institute of Zoology point to a peptide from centipede venom having the potential to be a more effective painkiller than morphine, possibly without some of the side effects, such as addiction. The Chinese red-headed centipede, which produces the venom, is a pretty significant size, coming in at a whopping 20cm long.



The Brazilian wandering spider is the world's most venomous spider

ABOVE These images of a canine soft tissue sarcoma show the use of 'tumour paint' to aid surgeons in the removal of cancerous cells

LEFT The deathstalker scorpion's venom is used to make tumour paint

GETTY IMAGES X3, ALAMY

SEA ANEMONES

TARGETS: Multiple sclerosis, rheumatoid arthritis, psoriasis and lupus

Native to the Caribbean, the sun anemone uses stinging cells in its tentacles to deliver venom to its prey, stunning small fish and other sea creatures before shovelling them into its mouth. Anemone venom peptides continue to pique the interest of scientists. One promising compound forms the basis of an experimental drug called dalazatide that's ready to undergo the second phase of clinical trials for treating autoimmune disease. Instead of suppressing the whole immune system like existing drugs, it very selectively blocks an ion channel in the particular type of immune cells that go haywire in autoimmune diseases such as multiple sclerosis, rheumatoid arthritis, psoriasis, and lupus. Kineta, a Seattle-based biotechnology company, is developing the drug.

The last known human fatality from a Gila monster bite was in 1939

LIZARDS

TARGETS: Diabetes

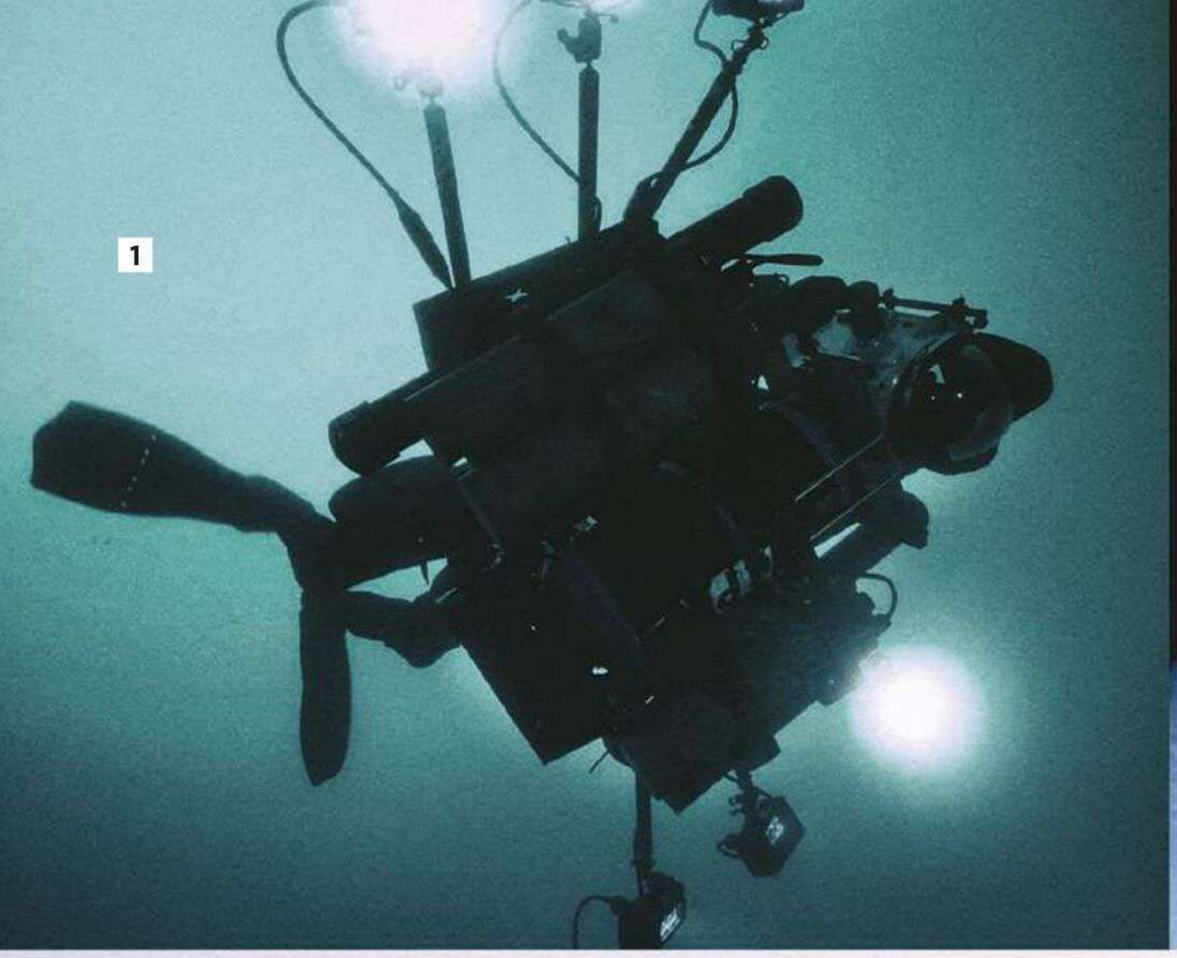
Heard of the Gila monster? These lizards are the biggest in the US and possess venomous saliva. They eat as little as three big meals a year, while managing to keep their blood sugar stable. Back in the early 1990s, researchers discovered a component in the lizard's venom that mimics the activity of a human hormone that stimulates insulin release when blood sugar levels rise. Exenatide, an injectable drug based on the toxin, helps people with diabetes maintain healthy glucose levels and even lose weight. **SF**

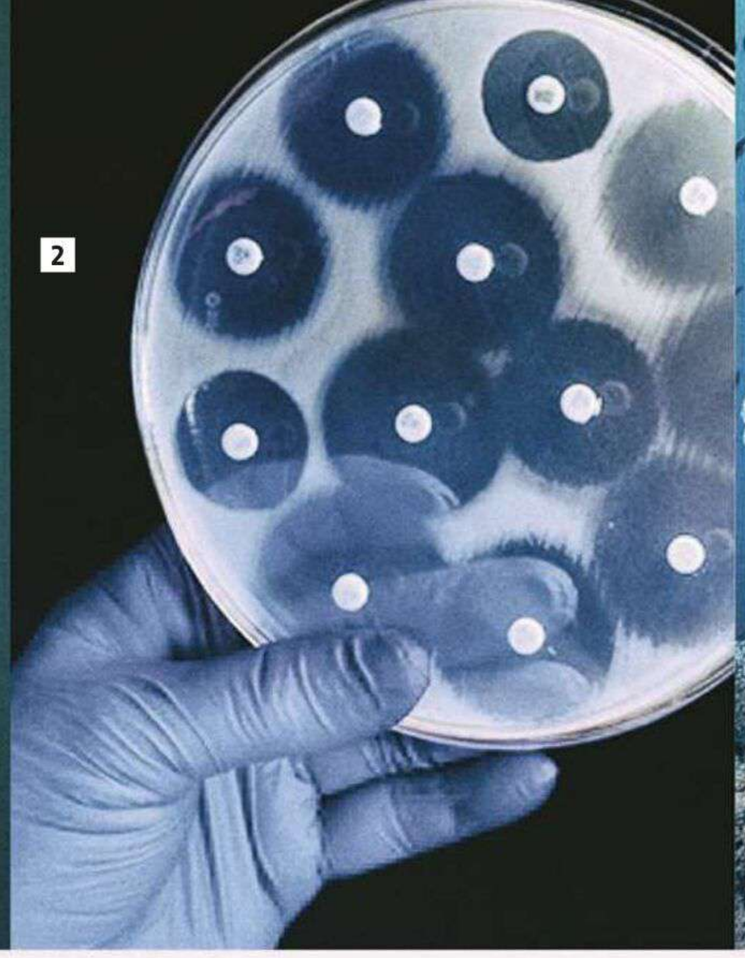
by **KATH NIGHTINGALE**

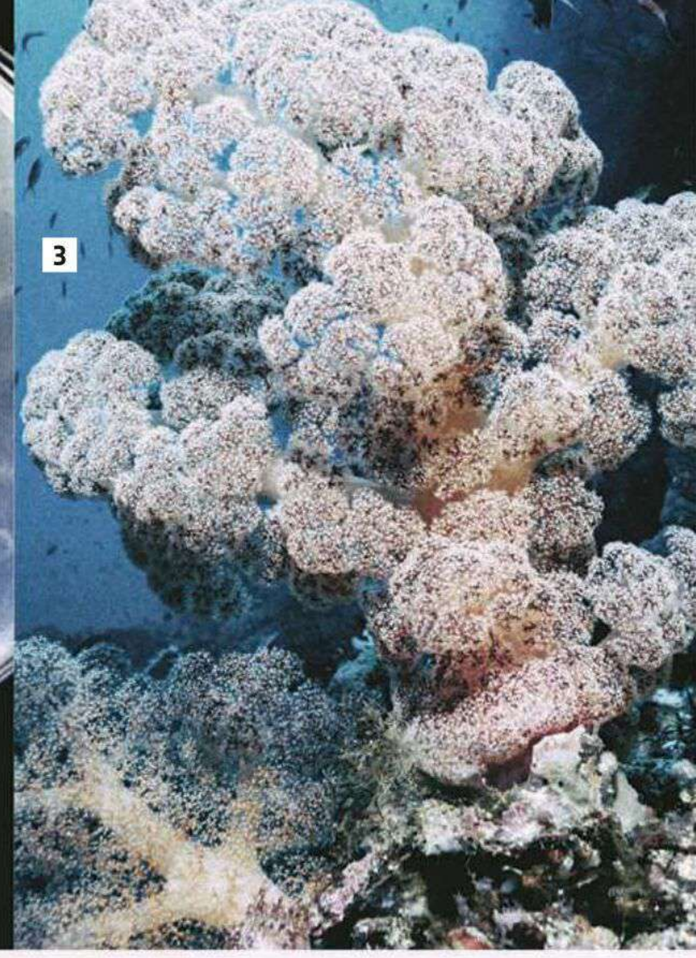
Kath is a freelance science writer with a background in molecular and cellular biology.

DISCOVER MORE

Visit the BBC Science Focus *website to see our gallery of the most venomous animals on the planet* ***bit.ly/venomous_animals***







RAIDING THE OCEAN'S MEDICINE CABINET

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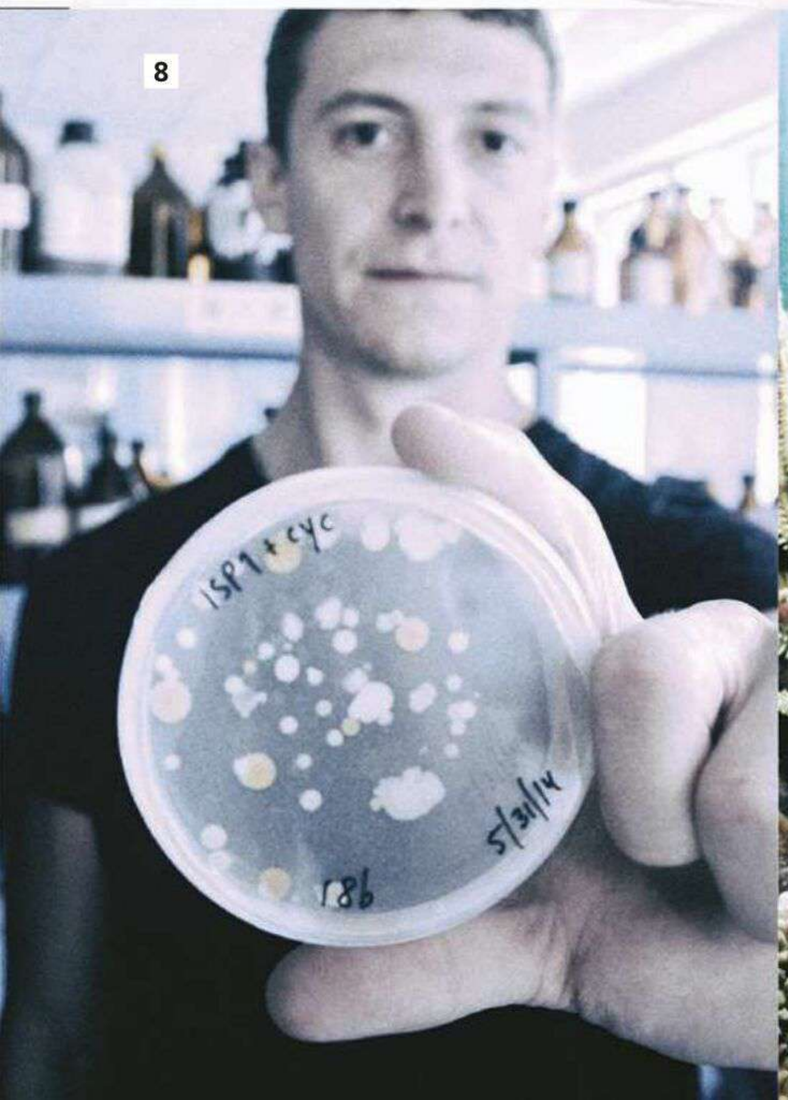
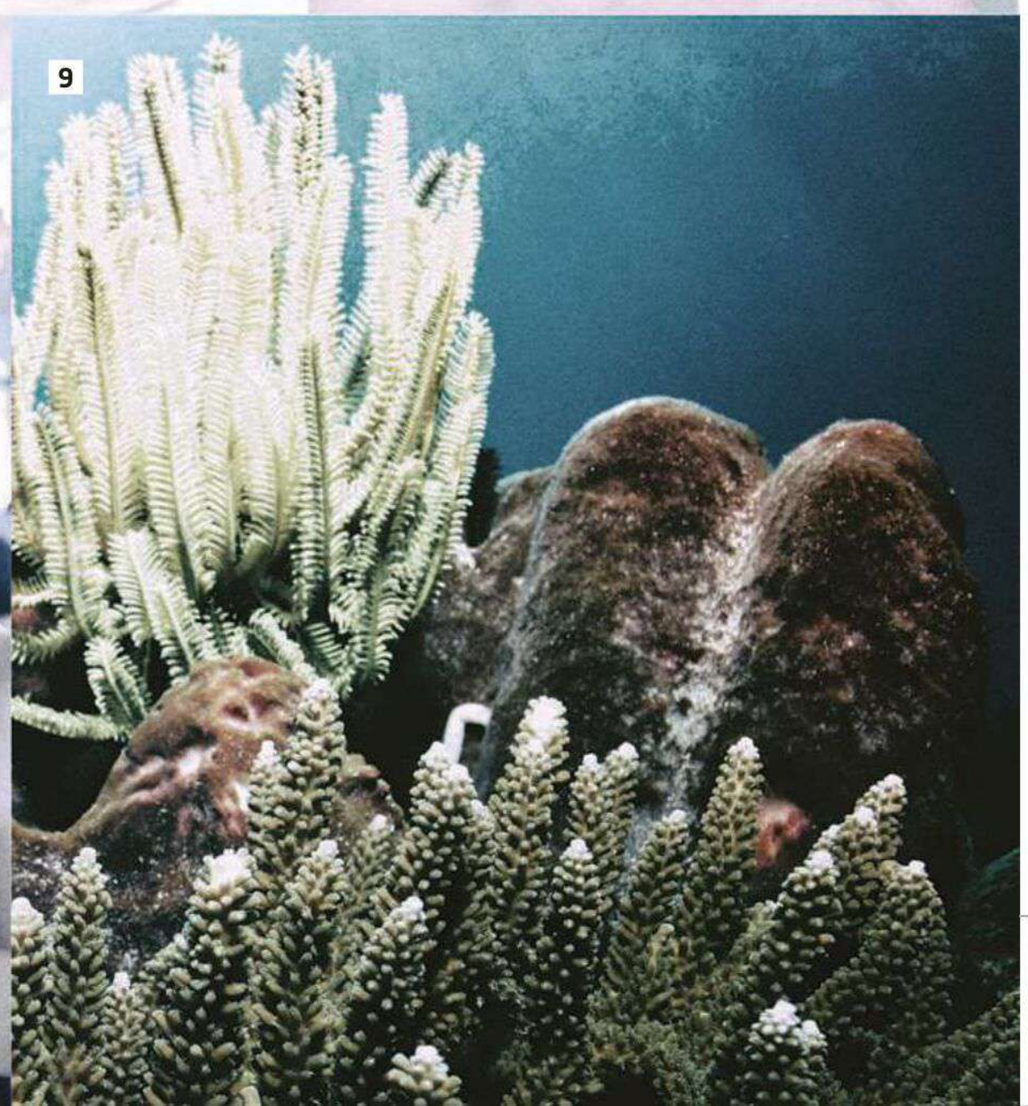




Antibiotics are losing their effectiveness against disease. But the world's waters could be full of new drugs, just waiting to be discovered

by HELEN SCALES

Mud and sponges probably don't feature highly on most scuba divers' bucket lists. But scientist and explorer Brian Murphy, based at the University of Illinois at Chicago, has his sights set on the sediments lurking at the bottom of lakes and the gooey animals clinging to submerged shipwrecks. And for good reason. He recently brought back a blob of mud from Lake Michigan and found it contained bacteria that make two previously unknown molecules. Lab tests showed that this class of compounds is lethal to the bacterium that causes tuberculosis, a disease that existing drugs are struggling with. "For millions of years bacteria have fought one another," says Murphy. "We're just harnessing that power."

Around the world, superbugs are on the rise. There have been a number of patients in recent years who have been found with strains of *E. coli* that's resistant to many antibiotics, including drugs that doctors only use as a last resort. It's an alarming trend in which bacteria are gaining the upper hand in their battle against the antibiotics we use to kill them, hastened by the world's overuse of these drugs.

"The way to combat drug resistance is to find new chemistry," says Murphy. He's

one of many modern-day prospectors who are searching for that new chemistry underwater.

PLUMBING THE DEPTHS

From icy polar seas to scorching hydrothermal vents, and from coral reefs to inland lakes, the vast, aquatic realms covering seven-tenths of our planet are home to an immense diversity of life. They include many animals that evolved complex chemical defences, along with a profusion of microbes; it is thought that around 90 per cent of oceanic life is microscopic. From among these creatures, researchers are uncovering molecules that could form the basis for new medicines.

Tapping the natural world for pharmaceuticals is nothing new – pop an aspirin and your headache will be soothed by a substance that was discovered in willow tree bark. With the rising tide of drug resistance, the hope is that nature has plenty more in its medicine cabinet for us to dip into. The trick is sifting through all those potent chemicals to find the ones that could fight disease.

"It's no secret that there's an incredibly high failure rate in developing drugs," says Murphy. "It's really difficult to find a set of molecules that can target a specific disease and do it within the incredibly complex environment of the human body."

To help with this, Murphy is working to smarten up the sample collection process, as it's one of the few steps in drug development that hasn't seen a major revolution in recent decades. According to Murphy, looking for molecules in original places is an important part of drug development, so he decided to use a new resource altogether: the general public.

Chatting with recreational scuba divers gave Murphy the idea of searching shipwrecks for sponges. These unprepossessing animals spend most of their lives stuck in place, sifting the water for food and taking on hordes of bacteria. "Bacteria can constitute up to 30 or 40 per cent of sponge biomass," Murphy explains. Freshwater sponges are a common sight across the USA's Great Lakes but almost nothing is known about them. Rather than go out himself and gather sponges – a time-consuming and expensive business – Murphy piloted a citizen science project asking divers to collect tiny samples for him

"The hope is that nature has plenty more in its medicine cabinet for us to dip into"

PREVIOUS PAGE

1 Diving the Great Lakes

2 Testing antibiotics in the lab

3 Animals on coral reefs have evolved interesting chemical defences

4 One of Brian Murphy's students leaps into the water to hunt for new drugs

5 The Great Lakes in the US are a popular dive spot as they contain hundreds of well-preserved shipwrecks

6 Michael Mullowney (left) and Brian Murphy processing deep-sea sediments

7 Gathering Icelandic algae for research

8 Brian Murphy with bacteria he's collected – some of these colonies contain a specific group of bacteria that's widely used in antibiotics

9 Bioprospectors first looked to coral reefs in the 1950s

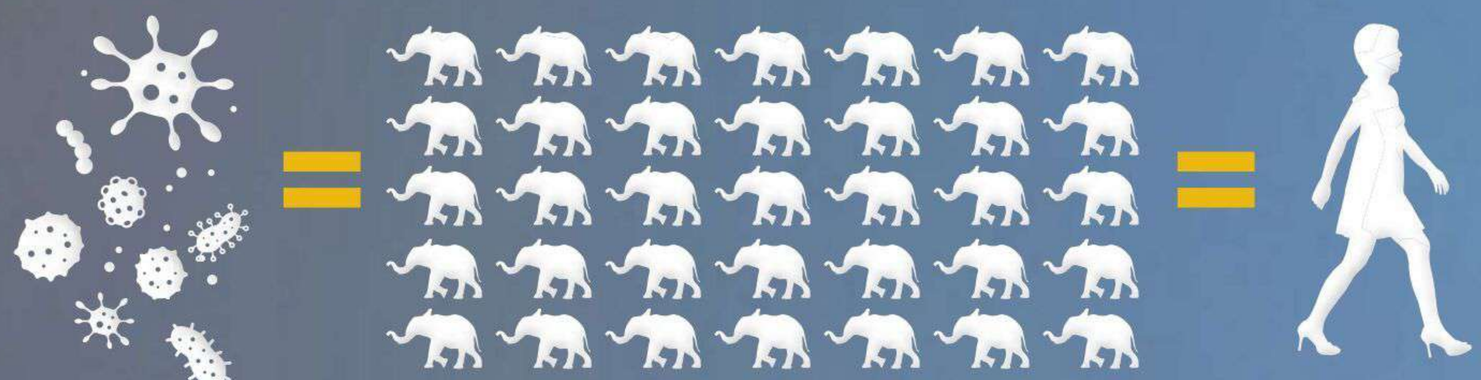
ABOVE The Great Barrier Reef spans 344,400km^2 – that's a lot of area to search for potential drugs

RIGHT Shipwrecks act as artificial reefs and become colonised with many species

GETTY, FLPA

BUGS AND DRUGS

We have a complicated relationship with microbes...



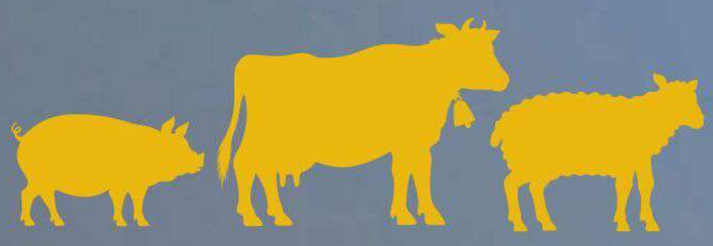
Microbes living in the ocean collectively weigh the equivalent of 35 African elephants for every person alive today.

In the last 30 years, around half of all new medicines released have been based on molecules found in the natural world.

£69,000,000,000,000

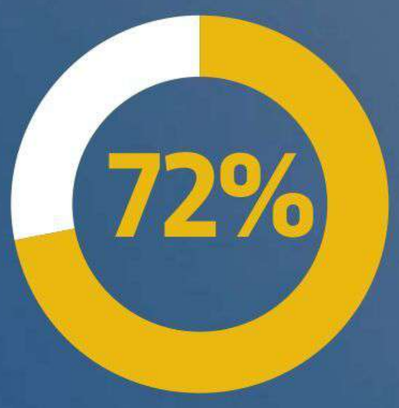
£69tn is the estimated annual cost of global inaction against antibiotic resistance by 2050.

By 2050, 10 million people could die per year (or roughly one every three seconds) if no action is taken to combat antibiotic resistance. That's more than the death toll from cancer and diabetes combined.

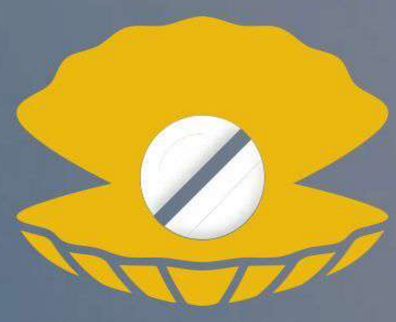


63,000 tons

Roughly half of all antibiotics used worldwide are given to food-industry animals to prevent infection and speed up growth rates.



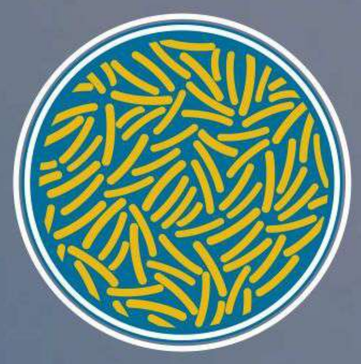
In a survey of 139 academic studies, 72 per cent showed a link between antibiotic use in farm animals and drug resistance in humans.

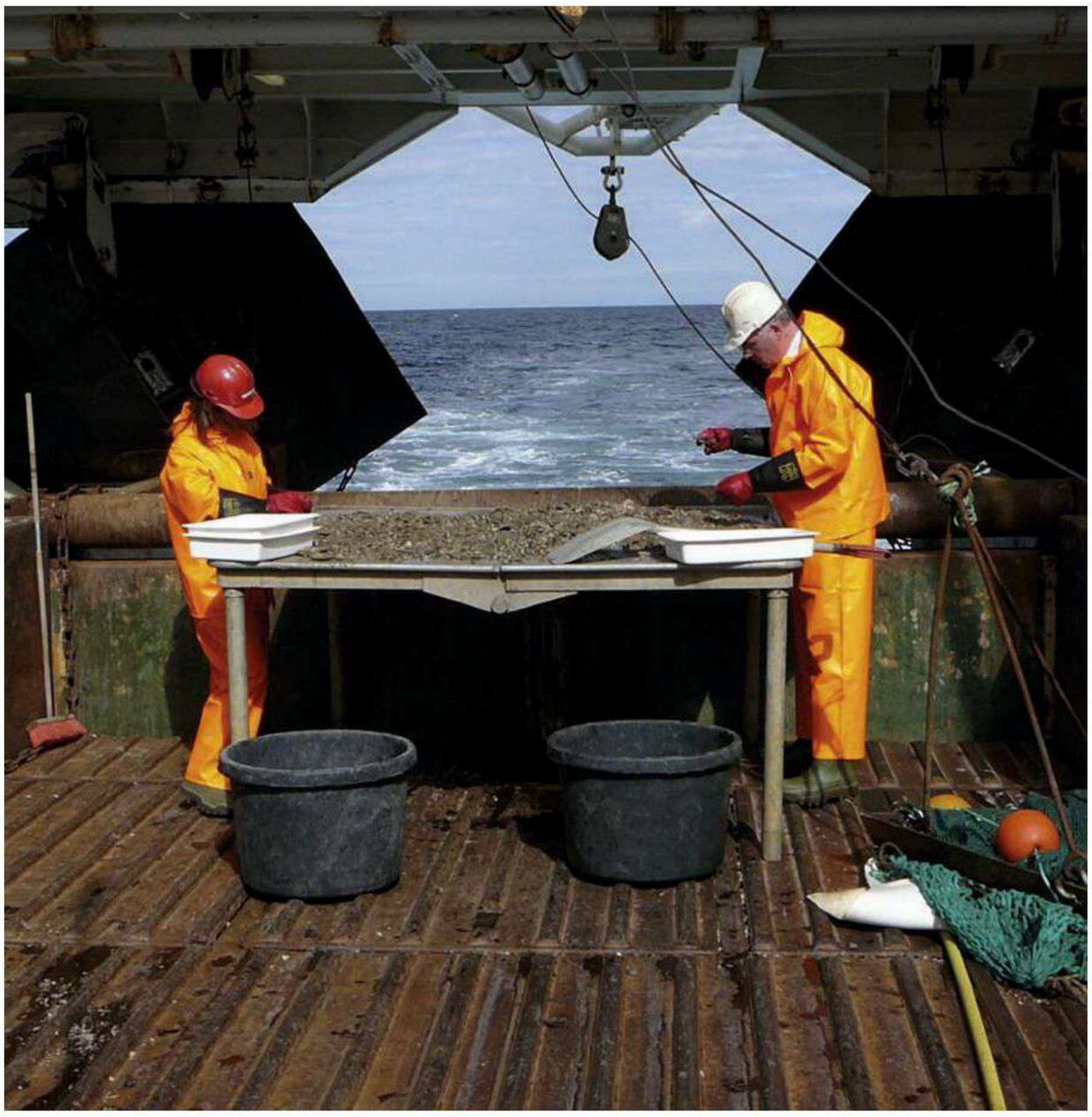


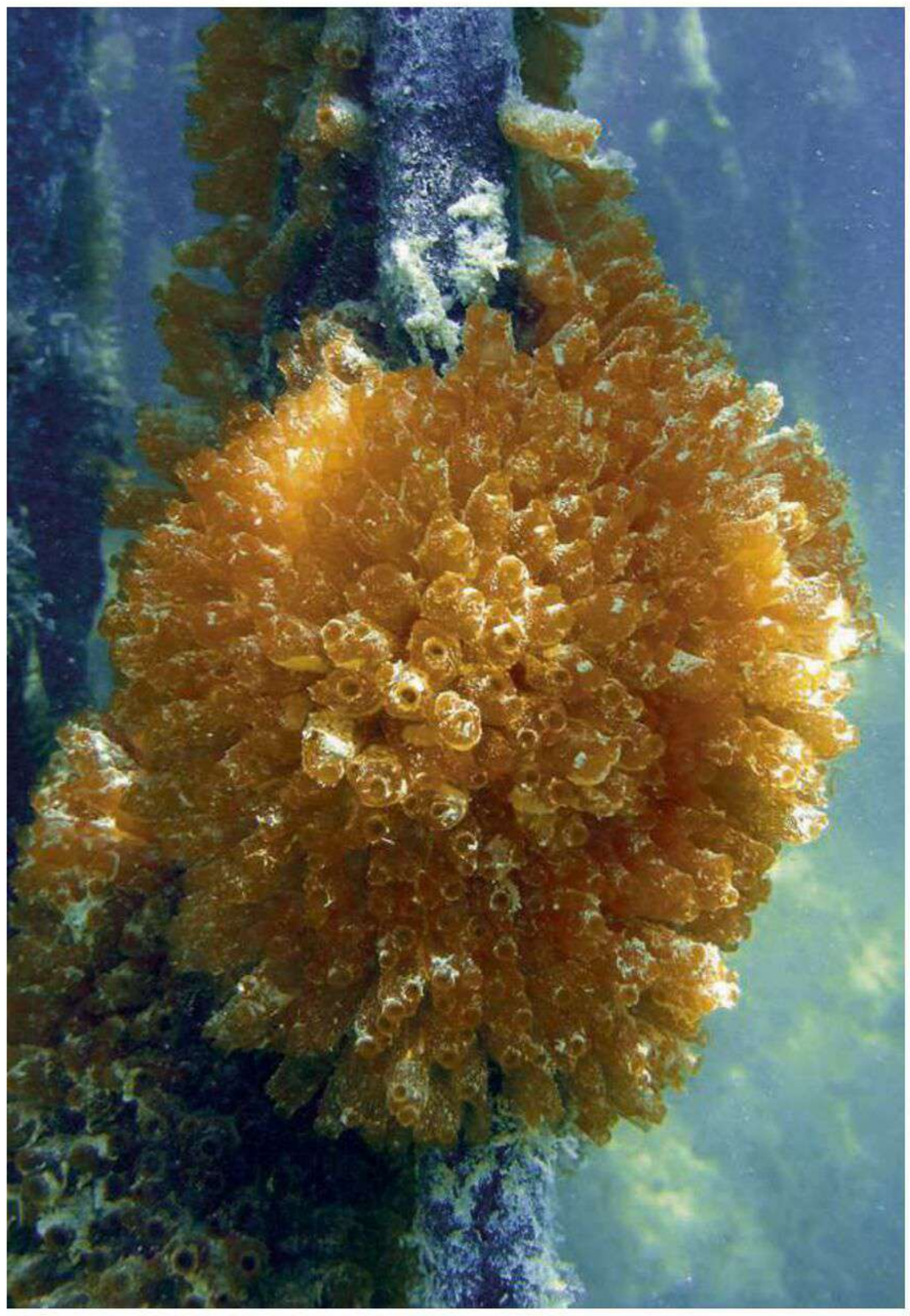
In 2011, the global market in drugs initially discovered in the sea was worth around $4.8bn.

In the US, between 1997 and 2010, 60 per cent of cases of sore throats were treated with antibiotics, even though only 10 per cent were caused by bacterial infection, at a cost of $500m.

Vancomycin was introduced in 1972 against drug-resistant strains of 'superbugs'. After seven years, bacteria began evolving resistance to the drug.







ABOVE PharmaSea researchers scouring through oceanic mud

ABOVE RIGHT Some sea squirts contain cancer-fighting agents

while they're out and about. He sent out collecting kits in and got a great response, receiving more than 40 nubbins of sponge in the mail.

In 2016 he rolled the project out across the Great Lakes and hopes to sample as many sites at possible. Ultimately, Murphy wants to map the distribution of sponges and bacteria across the lakes so that future efforts can be more effective and will zero in on fruitful spots, both in the Great Lakes and beyond.

DIVERSE OCEANS

When bioprospectors first turned to the oceans in the 1950s, their initial targets were coral reefs. These bustling ecosystems, packed with species, are a logical place to look and they've yielded many natural products, including some that made it to the end of the drug development pipeline. Early on was chemotherapy agent cytarabine, approved in the US in 1969 and originally found in a sponge on a Florida Keys reef. Another cancer-fighting agent called trabectedin, from a Caribbean sea squirt, has been used in Europe since 2007 and in the US since 2015.

Elsewhere, other researchers are hunting for novel chemistry even further beneath the waves. An international team called PharmaSea, led by Prof Marcel Jaspars, is searching for new antibiotics in the deep sea, including at the bottom of trenches – the deepest parts of the oceans. Jaspars describes these as 'negative islands' sticking down into the seabed, instead of pointing up. "It's possible there have been millions of years of separate evolution in each trench," he says. Jaspars and his collaborators send unmanned probes miles down into the depths to bring back mud loaded with unique bacteria. Techniques for keeping these extreme creatures alive in the lab have advanced in recent years, so experiments can be carried out. According to Jaspars, they've done around 100,000 tests, with targets including the so-called ESKAPE pathogens. This group of six bacterial strains are showing growing resistance to multiple existing antibiotics.

Ultimately, the PharmaSea team aims to narrow down two compounds that can be produced at a larger scale and put forward for pre-clinical trials. So far, their most promising finds are compounds that could be effective against diseases of the nervous system, in particular epilepsy and Alzheimer's disease.

BENEFITS FOR ALL?

But who owns these discoveries from the deep? The word 'bioprospecting' usually has a negative connotation. At worst, it brings to mind indigenous people giving away their knowledge of traditional medicines and receiving little reimbursement.

Thankfully, things have moved on in recent years, and protocols for sharing benefits are now commonplace. Prior to collecting anything, researchers will generally enter written agreements with the country of origin. In 2010, the international Nagoya Protocol came into

PHARMASEA, SEAN NASH, BILL BAKER, CENTERS FOR DISEASE CONTROL AND PREVENTION, HOWARD LASKER, WESLEY OOSTHUIZEN, GETTY X

UNDERWATER PHARMACY

These creatures contain chemicals that could beat cancer, MRSA, and more

HORSESHOE CRABS

The blood of these arthropods is packed with amoebocyte cells that react to tiny traces of bacteria. Their blood has been used for the last 50 years to test equipment and vaccines for contamination.

CONE SNAILS

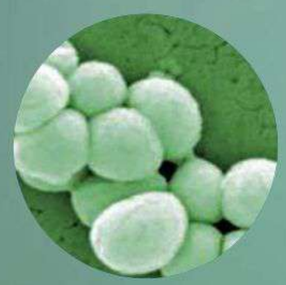
The stings of these molluscs contain conotoxins. There is already a conotoxin-based painkiller that's more potent than morphine. There are also cancer and diabetes treatments on the horizon.

SPINY STARFISH

This starfish's body is covered in slime consisting of 14 per cent carbohydrate and 86 per cent protein. The substance is being investigated as a treatment for arthritis and asthma.

PUFFERFISH

These fish contain tetrodotoxin (or TTX). This is what makes fugu (a delicacy made from pufferfish) a risky dinner. TTX is being developed as a treatment for the pain suffered during chemotherapy.



MICROCOCCUS LUTEUS

This bacterium produces a pigment called sarcinaxanthin that can block long-wavelength UV radiation. This could be used in the development of more effective sunscreens.

DENDRILLA MEMBRANOSA

This sea sponge contains a molecule called darwinolide. This substance has been found to be effective against the drug-resistant MRSA 'superbug', which can often cause problems in hospitals.

ELYSIA RUFESCENS

This species of sea slug has a wide distribution. It contains a substance called kahalalide F, which is currently under investigation as a potential tumour-fighting agent.

"It's possible there have been millions of years of separate evolution in each trench"

effect, making such agreements a legal requirement. But not everyone is signed up to Nagoya – the US is notably absent.

The high seas begin 200 nautical miles from shore and don't technically belong to anyone, making them difficult to police. Currently, the UN Convention on the Law of the Sea (UNCLOS) covers certain activities including deep-sea mining and laying cables, but it says nothing about biodiversity. Formal discussions got underway in March this year to amend UNCLOS to encompass bioprospecting. Various views are on the negotiating table. "The G77 and China believe that it should be the Common Heritage of Mankind, which would mean everybody could benefit," explains Jaspars. The idea is that one single nation or company shouldn't be allowed to solely benefit.

On the other hand is the concept of Freedom of the High Seas, backed by the US and Norway, which would give any nations freedom to bioprospect in the high seas, just as anyone can fish there. They could research anywhere and hold on to the profits. Other groups, including the EU, are keen to find a solution. It's likely to be several years until bioprospecting in the high seas becomes regulated.

NEW WAYS AHEAD

Back in the lab, Murphy's tuberculosis-busting molecules are entering the next round of tests to see if they could lead to new medicines. Even if they don't, Murphy is confident they will still be useful. "They showed very selective antibacterial activity towards tuberculosis," he says. Other bacteria were left untouched. Finding out exactly how these molecules selectively kill the tuberculosis bacterium could reveal vital information about the disease itself and perhaps point the way towards effective medicines.

But bioprospectors will have to hurry. In recent years, the ailing Great Barrier Reef has made headline news around the world, and human activities continue to threaten the health and biodiversity of Earth's oceans, rivers and lakes. Let's hope we can find the drugs and cures we need before our planet's waters become irrevocably sickened. **SF**

DISCOVER MORE

BBC RADIO 4 *Listen to* The Life Sub-Aquatic *with Helen Scales about the human obsession with living beneath the waves at* ***bit.ly/living_under_water***

by **HELEN SCALES** *(@helenscales)*
Helen is a marine biologist and writer. Her recent books include Eye Of The Shoal *(£16.99, Bloomsbury Sigma) and* Octopuses *(£8.99, Penguin).*

Students excavate a corpse at the body farm at Texas State University

FBI PHOTO LIBRARY. ILLUSTRATION: MICHAEL HADDAD

DOWN ON THE BODY FARM

Corpses can tell you a lot – if you know how to read them. And just like language, decomposition is dependent on location. Which is why researchers are keen to start studying the dialect of decay here in the UK

by ROB BANINO

Dr Anna Williams wants to watch you rot. It's nothing personal; it's for science, specifically the science of taphonomy, which is the study of decay and fossilisation. By monitoring how corpses decompose, she hopes to increase our understanding of the subtleties of the process and improve the accuracy with which we can locate and identify dead people, and determine their time of death.

In order to do this, Williams, a forensic anthropologist at the University of Huddersfield, has been keen to establish a human taphonomy facility in the UK. And in 2019 it was announced that forensic scientists, led by Williams, would be working with the British military to open the UK's first body farm. However, specific details such as location, are being kept tightly under wraps. There are already nine such facilities – colloquially known as 'body farms' – around the world: seven in the US, one in Australia and another in the Netherlands. So why do we need one here?

"What we know about decomposition has come out of the American facilities," explains Williams. "Before the first one opened in 1981, we really didn't know very much about how bodies decompose in different conditions. The research that's been going on since then has really boosted our knowledge.

"And one of the things we've learned is that decomposition is incredibly dependent upon local conditions: the surrounding temperature, rainfall,

“TYPICALLY, WRAPPING A BODY WILL ACCELERATE DECOMPOSITION BUT IT ALSO DEPENDS ON IF IT’S BURIED OR NOT”

humidity, soil type, ecology, insects, scavengers… it’s all dependent on these variables. So, the information coming out of the existing facilities is very useful but it’s not directly applicable to forensic cases in the UK.”

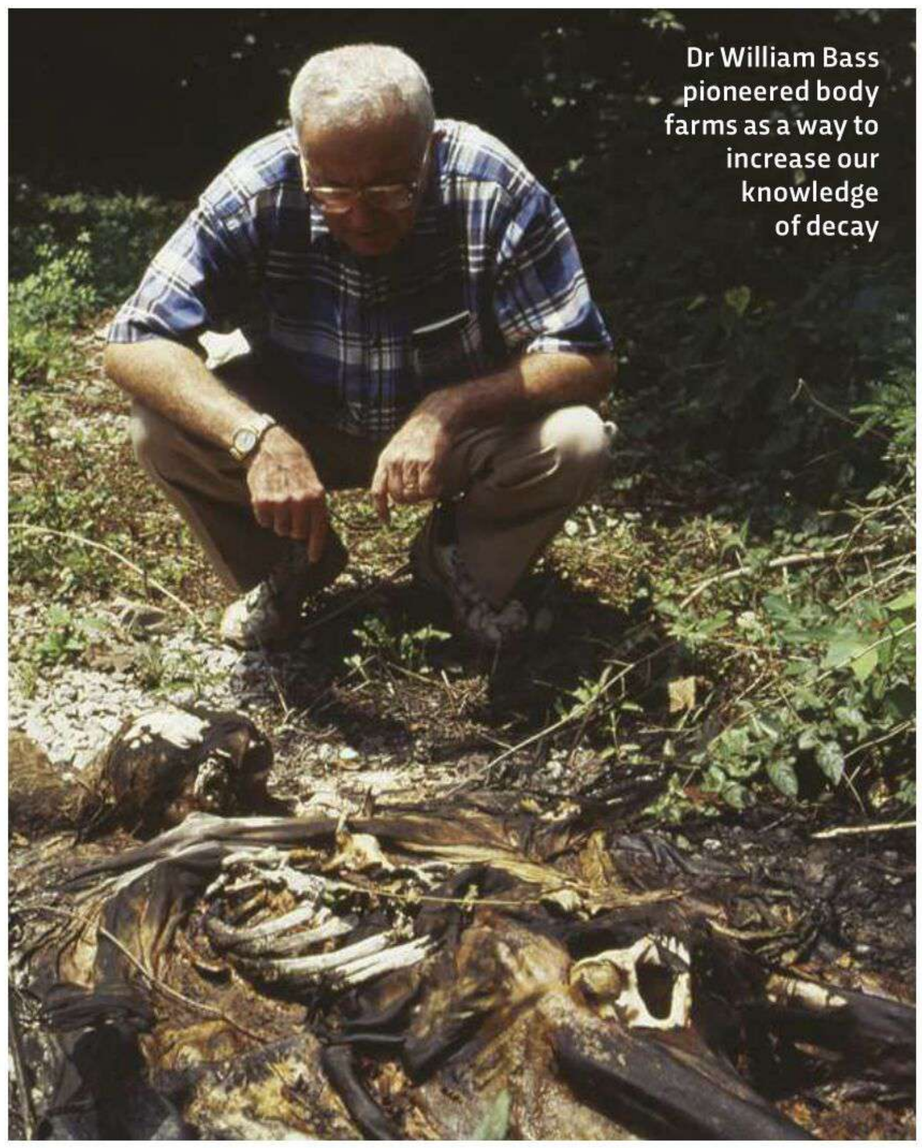
In short, people in the UK don’t decay in the same way as they do elsewhere. In fact, people don’t always decay the same way in the same country. And we wouldn’t know that if it wasn’t for the pioneering work of forensic anthropologist Dr William Bass.

LYING IN THE GRAVE

Bass founded the first human decomposition research facility at the University of Tennessee after recognising how misleading the decay process could be. The realisation came in 1977 after local police contacted Bass and asked him to examine some human remains they’d found in a disturbed grave. The corpse’s head was missing, but based on the remaining flesh and bones it was originally determined that the remains belonged to a white male in his mid-to-late 20s who’d been dead for about a year.

However, Bass’s examination revealed something astounding: the corpse was older than everyone thought. A lot older. It was actually the body of the Confederate soldier, Colonel William Shy, who’d been dead for over a century. The remains were so well preserved because they’d been embalmed and buried in an airtight coffin. What the police had found wasn’t a killer’s attempt to hide the body of a recent victim but the remains of a corpse that had been dug up by graverobbers. The confounding nature of Colonel Shy’s corpse led Bass to an epiphany: we needed a far better understanding of human decomposition and the factors that affect it. We needed to study it closely, and to do that we’d need decomposing bodies and somewhere to watch them fester.

That place ended up being a 2.5-acre (10,000m²) fenced-off wooded area in Knoxville, Tennessee,



Dr William Bass pioneered body farms as a way to increase our knowledge of decay

BREAKDOWN

Left unburied and uncovered, here’s what happens to a body…

The fresh stage can last a few days to a week. Rigor mortis initially sets in and cells break down as the lack of oxygen and nutrients prevents them from replenishing themselves.

When bacteria in the gut can no longer be kept in check, they start to reproduce and feed on the body. This produces gas that causes the abdomen to bloat.

FBI PHOTO LIBRARY, SCIENCE PHOTO LIBRARY, DANIEL WESCOTT ILLUSTRATION: MICHAEL HADDAD

which today is the outdoor decomposition research facility of the University of Tennessee's Forensic Anthropology Center.

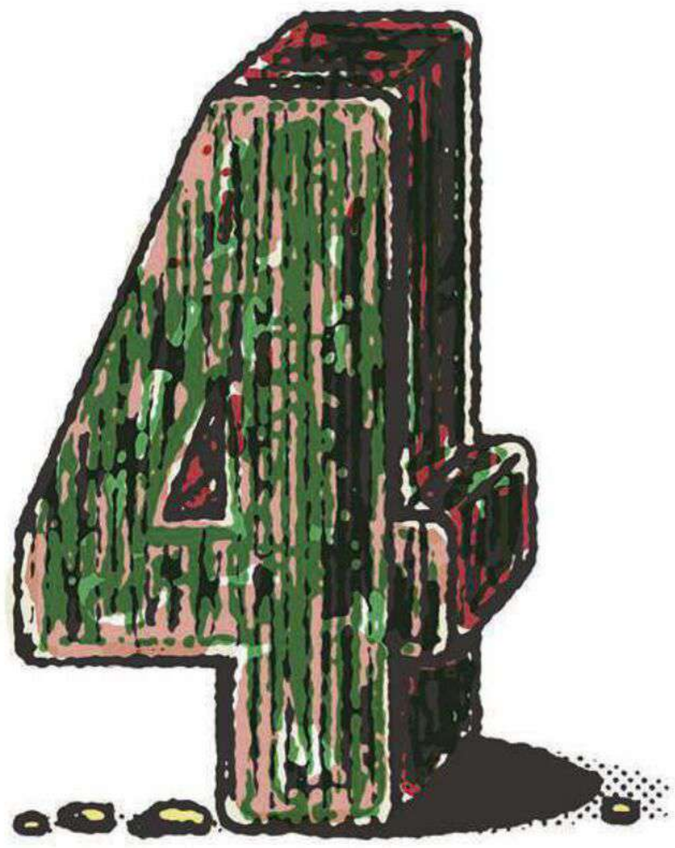
Since the facility opened in the 1980s, Bass and his colleagues have scrutinised the decay of thousands of cadavers in various states: buried, unburied, whole, dismembered, hidden in car boots, wrapped in carpet and entombed in concrete. And the contribution they've made to our ability to locate and identify human remains, and more accurately infer their time of death, is unquantifiable.

Students at Texas State University clean bones after the soft tissue has decomposed. The bones will be sent to the university's permanent skeletal collection

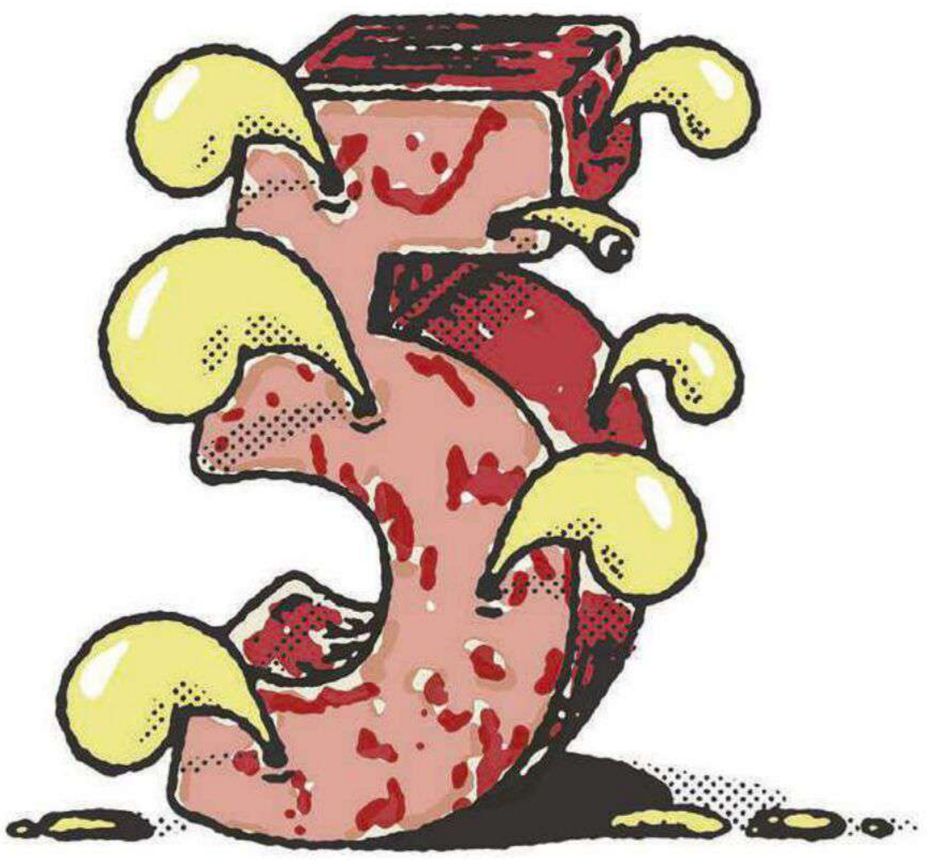
DEATH FROM ABOVE

The progress made at Tennessee inspired other US universities, like Texas State University, to build on Bass's example. Dr Daniel Wescott is the current director of the Forensic Anthropology Center at Texas State (FACTS), which opened in 2008. "We have lots of graduate students researching different aspects of decomposition, such as what happens if you wrap a body in a specific material," he says. "Tarps and carpets tend to accelerate the rate of decomposition as they retain heat and moisture, and provide protection for the insects so that they feed a little faster. Typically, wrapping a body will accelerate the decomposition but it also depends on if it's buried or not."

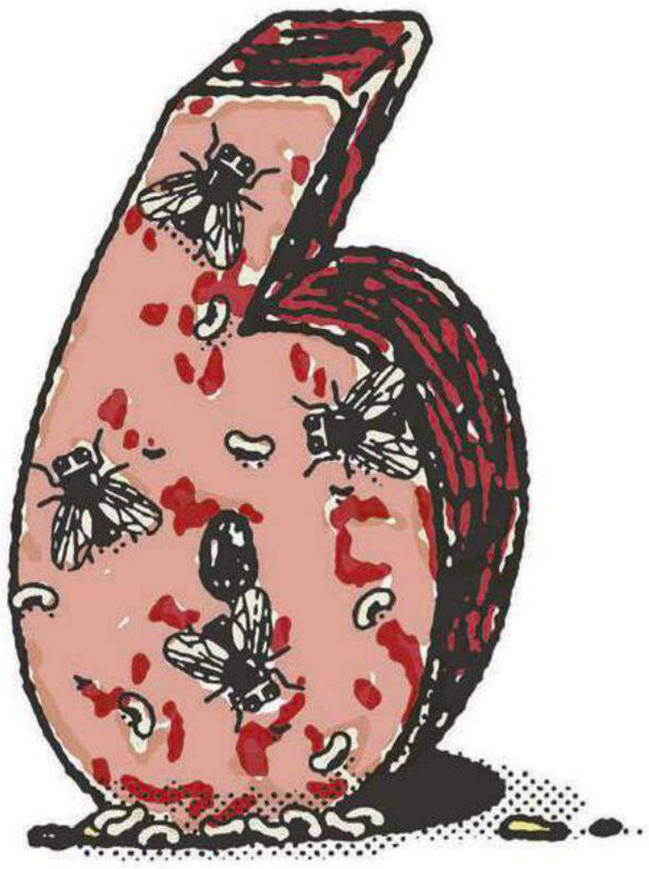
Gas building up increases pressure within the body, pushing fluids in between the layers of skin and causing the outer layers to slough off.



With no oxygen to bind to, haemoglobin in the blood binds to sulphur instead, filling the arteries and veins with a greenish-black substance. This gives the flesh an appearance known as 'marbling'.



Increasing pressure forces the body's fluids and liquefied organs out of any available orifice. Eyeballs can be dislodged and bodies have even been known to explode.



Chemicals released by the body attract flies, which lay eggs in and around the orifices. Soon after, maggots hatch and begin feeding on the body's flesh and organs.

Other insects, such as beetles, are attracted to the body, as well as small birds looking to feed on them. Local scavenging animals will also appear to pick the flesh off the bones.

The final stage is skeletonisation, when the soft tissue is fully lost. Wind, rain, erosion and abrasion take over and the bones are disarticulated over the following months and years.

They're also looking at ways to use drones to find bodies. Until now, searches for missing bodies have relied on manpower, specially trained sniffer dogs and ground-penetrating radar devices. But, as Wescott explains, FACTS is testing ways to locate corpses using drones. "In the early stages of decomposition you've got a lot of chemical reactions going on, you've got bacteria proliferating, you've got maggot activity… and all that generates heat. We can use infrared cameras on the drones to pick up that heat.

"Later on, a skeleton's not going to give out heat but we can use near-infrared photography to pick up what's called a 'cadaver decomposition island'. This is what you get when the fluids seep out of a decomposing body into the surrounding soil. We can pick up the areas of enriched soil because it reflects light differently."

But as useful as this research is, no one can pretend the climate in the US is anything like that of the UK. "Environmental variables have a big influence on the rate at which a body decomposes. So, when you're talking about trying to calculate how long somebody's been dead, the basic principles that come out of Texas apply but the specific rate probably wouldn't apply to Europe," says Westcott. Which brings us back to Williams and the importance of opening the human facility this side of the Atlantic.

CEMETERIES AND SENSIBILITIES

Williams had previously taken steps to advance the understanding of decomposition in the UK by opening an animal taphonomy facility in Cranfield University in 2011. But recent studies have shown that the pigs, rabbits, mice, sheep and deer used in such labs aren't suitable analogues for humans because they have different gut bacteria, medical conditions, diets and lifestyles. To put it another way, pigs don't smoke, get diabetes or overindulge on fast food, alcohol or drugs, all of which can affect the way a body breaks down. And if the information generated using animals isn't comparable to humans, aside from the doubt it casts on any research, it can also be more easily undermined if it's used in testimony during a trial.

"A SKELETON'S NOT GOING TO GIVE OUT HEAT BUT WE CAN USE NEAR-INFRARED TO PICK UP A 'CADAVER DECOMPOSITION ISLAND'"

Hence the need for a human facility in the UK. Consideration will be given regarding ways to mitigate any offence an outdoor lab containing rotting corpses may cause. "One thing that we might do is try a staggered approach so that we start with a facility more like the one in Amsterdam, which is called a 'forensic cemetery' because the bodies are buried," she says. "You can't see the bodies as they're not on the surface and that's perhaps less objectionable, more readily acceptable."

In such a scenario, monitoring equipment and possibly even viewing windows would be installed underground to study the cadavers as they decompose. But it may actually be the perception of the public's attitude towards such a facility that's mistaken. A survey carried out by Williams suggests people are in favour of a human taphonomy facility in the

DISCOVER MORE

BBC NEWS *Watch a short BBC video about Australia's body farm at* ***bit.ly/body_farm***

Listen to an interview with Dr Anna Williams on the Science Focus Podcast. *Visit* ***sciencefocus.com/sciencefocuspodcast*** *or subscribe on iTunes, Acast, Stitcher, or your favourite podcast app.*

DANIEL WESCOTT ILLUSTRATION: MICHAEL HADDAD

At Texas State University, some corpses are kept inside cages to protect them from scavengers

UK, and she's already getting offers from people wishing to donate their bodies. When the forensic cemetery opens here, aside from the research and training benefits it could provide, Williams believes it would also enable more people's dying wishes to be granted.

"At the moment lots of people want to donate their bodies to anatomy schools for teaching and dissection but often they're turned away because they have conditions that mean they're unsuitable. We think that at a taphonomy facility we'd turn away fewer people because it wouldn't matter so much what conditions they had or what state their body was in."

In an ideal world, Williams hopes that donors will not only be able to choose what sort of research their body is used for, and for how long, but also what happens to their remains afterwards – whether they're kept as part of osteological collections or returned to their families for burial or cremation.

"[When the facility opens] there'll be a lot of setting up at the beginning," says Williams. It will be probably months or even years before we get the first experiments underway because there's so much testing to do at the site… You've got to find out what everything is like – the soil type, the vegetation, the humidity, the temperature, the shade, even the number of worms, birds and snails – we need to know about all that before we put the bodies in."

The facility will be off-limits and inaccessible to the public, so you needn't worry about stumbling across corpses on your daily walk… **SF**

by **ROB BANINO**

Rob is a Bristol-based writer and editor, specialising in science, technology and cycling.

OTHER THINGS TO DO WHEN YOU'RE DEAD

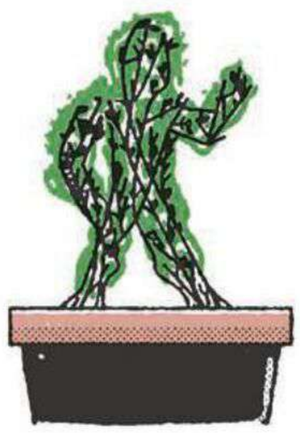
Donating your body to medical science is one way to make yourself useful after death. But what if you want to do something that's not so 'run of the mill'?

CRASH CARS

Car manufacturers like to demonstrate the efficacy of their vehicles' safety features by showing you slow-motion video of dummies getting thrown about during a collision. What they're less keen to publicise is that they've probably put dead bodies through the same tests to see how the impacts affect their internal organs.

PUT ON A SHOW

***Body Worlds* exhibitions feature real corpses and organs that have been preserved through plastination, a technique invented by German doctor Gunther von Hagens. If you're willing to go on display after your bodily fluids and soluble fat have been replaced by liquid plastic, you could donate your body to the Institute for Plastination.**



GROW A TREE

You can still make yourself useful after you've been cremated, depending on what happens to your ashes. Scattered on soil, your ashes will act as a general fertiliser. But if you want something more specific you can have them added to a Bios Urn, a biodegradable container that's packed with soil and used for tree seed germination.

RELEASE A RECORD

An audio recording of your voice, or music that held a special meaning for you, is one way that loved ones can treasure your memory. If, however, you'd like the keepsake to bear slightly more of your physical presence you can get andvinyly.com to press your ashes into the vinyl on which your voice and music is printed.

MASTERS OF DISASTER

CALLUM BENNETTS

Scientists are recreating extreme weather and natural disasters inside labs around the world. Their aim: to prepare for the next big catastrophes

by HAYLEY BENNETT

MAKING WAVES

← FLOWAVE, EDINBURGH

Capable of making 28m-high waves, Edinburgh University's FloWave is the world's largest circular wave and tidal tank. The 25m-wide, 5m-deep pool was built to test wave and tidal energy machines (which convert the ocean's energy into electricity), as well as for basic research on how waves are made at sea. Using 168 computer-controlled paddles, visible here around the edge, FloWave can produce waves and tidal currents in any direction. Recently, Edinburgh researchers teamed up with Oxford University academics to better understand how 25m-plus 'freak waves' can form when waves travelling in different directions cross paths. These giant waves are thought to have sunk many a ship over the centuries. The plume of water in this photo, however, is a 'party trick', and wouldn't occur naturally. Like a stone's throw in reverse, ripples made at the edge of the tank travel towards the centre, where they converge and shoot two tonnes of water straight up in the air.


整理＋整頓

DOUGLAS LEVERE/UNIVERSITY AT BUFFALO, MARIA KOLIOU/TEXAS A&M UNIVERSITY, SCANIA

SHAKE IT UP

← E-DEFENSE FACILITY, JAPAN

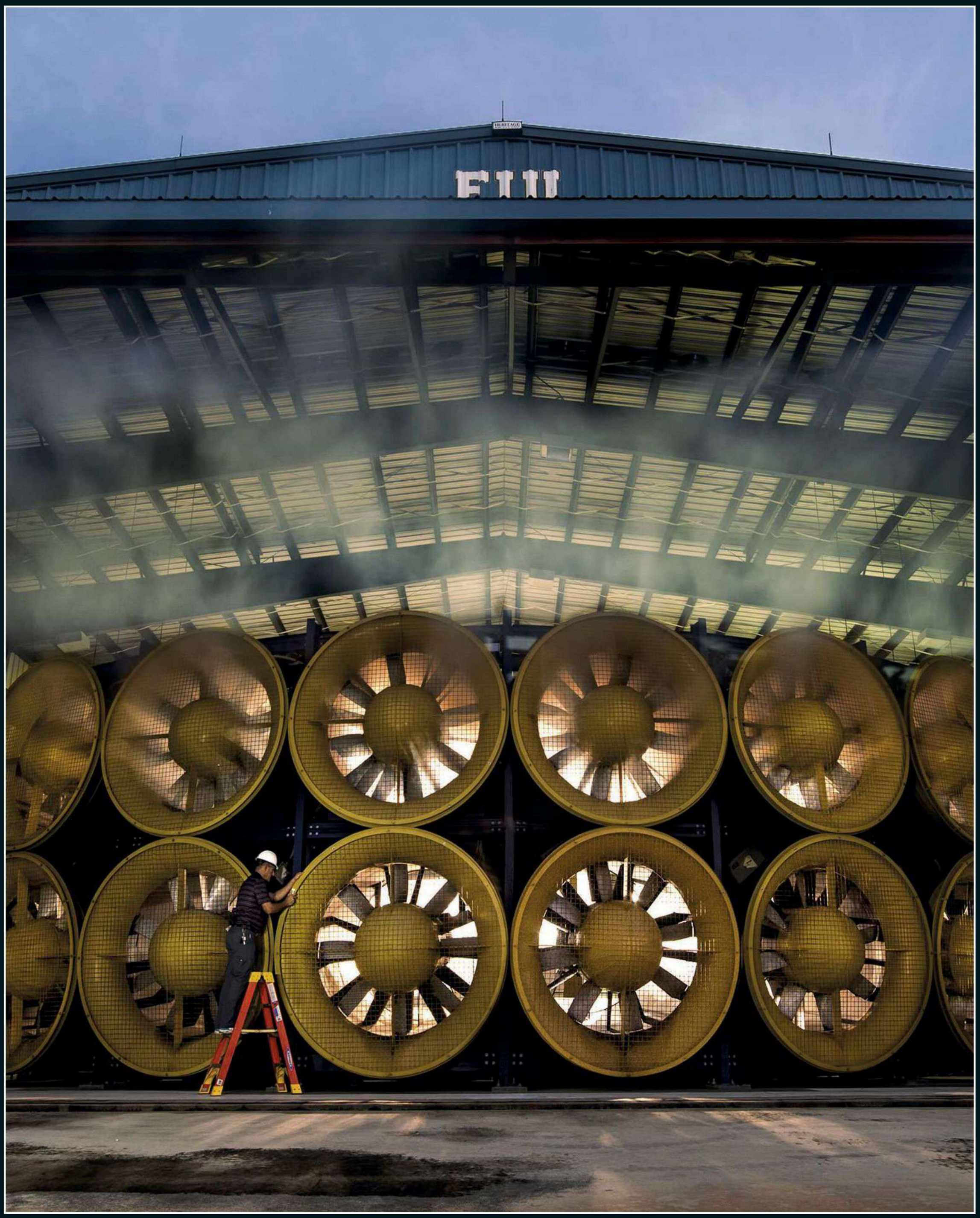
The ‘shake table’ at the E-Defense facility (‘E’ stands for ‘Earth’) near Kobe, Japan, is the largest in the world. The 20m by 15m platform hides an array of 24 pneumatic pistons, which are controlled by engineers to shake full-scale buildings in three directions, at earthquake-level intensities. When Texas A&M University engineer Dr Maria Koliou visited in February 2019, she got to wander around these fully furnished, wood-framed houses and then watched as her Japanese colleagues ran their shake programmes – one of which simulated the 6.9 magnitude Kobe earthquake that destroyed 150,000 buildings in 1995. “It was pretty impressive,” says Koliou. “I hadn’t seen a full-scale test before.” The right-hand building was even grounded in soil with pipes running through it, to get closer to real-life conditions.

The Japanese scientists surveyed the structural damage caused to the houses, with the aim of learning how building companies can better protect people’s homes during earthquakes.

ICE ICE, BABY

↑ SCANIA TEST FACILITY, SWEDEN

At this sophisticated climate facility in Södertälje, Sweden, you can control the weather. Developed by truck manufacturer Scania at a cost of £33m, it took three years to build and is intended for testing heavy vehicles in the harshest weather conditions. The snowdrifts in this picture were produced by snow cannons like those used at ski resorts, while a single 3.75m-high fan provides the wind for snow storms. On another day, conditions could be more akin to a desert heatwave, thanks to a temperature control system that goes as low as -35°C and up to 50°C. The humidity can range between 5 and 95 per cent, and even the droplet size of simulated rain is adjustable. Rollers under the parked vehicles allow the researchers to mimic speeds of up to 100km/h as they study variables such as driver visibility, windscreen wiper function, and the reaction of different components. Scania hopes that its facility will help improve fuel efficiency in demanding conditions, cutting down vehicles’ emissions.



FLORIDA INTERNATIONL UNIVERSITY, INSURANCE INSTITUTE FOR BUSINESS AND HOME SAFETY

SUCH A BIG FAN

← WALL OF WIND, FLORIDA

Together, the motors behind these massive fans provide the power of more than eight Mercedes Formula 1 racing cars at top speed. They're also capable of simulating hurricane winds strong enough to rival Katrina, the storm that devastated the city of New Orleans in 2005. Researchers at Florida International University use the Wall of Wind facility to test building materials and outdoor structures like solar panels that need to withstand strong winds. The fans are independently controlled and can rotate 1,800 times per minute, generating winds of up to 253km/h (equivalent to the most destructive type of hurricane – 'Category 5'). Test structures are placed on a turntable in front of the fans, before researchers beat a hasty retreat to view the action on-screen from the control area. Among other things, experiments have tested scaled-down bridge sections (to help with the hurricane-proofing of bridges), and the wind required to lift metal roofs off buildings.

BURNING UP

↓ WILDFIRE SIMULATOR, SOUTH CAROLINA

Wildfire spreads like... well, wildfire, in this specially designed wind tunnel in Chester County, South Carolina. This is part of a six-storey research facility belonging to the Insurance Institute for Business and Home Safety (IBHS). The tunnel is used to simulate what happens when burning embers are driven by wind to produce the 'ember storms' often seen in wildfires, which can be devastating to nearby buildings. On the right of the picture, embers – made in chambers filled with mulch and wood – are blown across the test space from metal ducts. The building sits on a rotating platform so that the embers can be blown from different directions. Researchers examine how the embers get into buildings through vents, and look at how decking and debris can help wildfires to spread. In this picture, plants below the front windows are acting as kindling, while the wooden step outside the front door is also adding fuel to the flames.

SHIVER ME TIMBERS

← DEBRIS IMPACT FACILITY, TEXAS

You can't shoot a bullet through a brick wall, but fire a piece of wood at it hard enough and you might have more luck. In the image to the left, the strip of wood shatters, but it isn't quite moving fast enough to break through the bricks. However, at 160km/h, it rips right through, as researchers at the Debris Impact Facility at Texas Tech University have demonstrated by firing a piece of wood from their pneumatic cannon. Even though a bullet shot from a gun moves faster, a strip of wood is heavier, so the impact is greater. This explains why debris thrown at high speed by a tornado can cause so much damage. The researchers use their cannon to simulate the impacts of flying debris in tornadoes travelling at up to 400km/h, testing storm shelters, safe rooms, doors and windows to their limits.

RECIPE FOR DISASTER

← UNIVERSITY OF BUFFALO, NEW YORK

How do you cook up volcanic lava in the lab? A team at the University of Buffalo in New York has the recipe down: take 45 litres of basaltic rock, put it in a furnace, bake for four hours until it reaches 1,316°C, then pour it into an insulated steel box. In this photo, volcanologist Dr Ingo Sonder stirs the lava. His experiments examine "the basic physics of what happens when water gets trapped inside molten rock". This could help scientists learn more about explosions like the one that triggered the Icelandic ash cloud event in 2010, when meltwater from a glacier flowed into the erupting Eyjafjallajökull volcano and threw ash 9km into the air, leading to the cancellation of nearly all European flights for five days. By injecting water into DIY lava, Sonder's team has discovered that spontaneous explosions are more likely to occur when water meets lava at a depth below the surface exceeding 30cm. At shallower depths, the water can escape as steam before it causes an explosion. SF

by **HAYLEY BENNETT** *(@gingerbreadlady)*
Hayley is a Bristol-based science writer and editor. She is the co-author of The Big Questions In Science *(£5.99, Andre Deutsch).*

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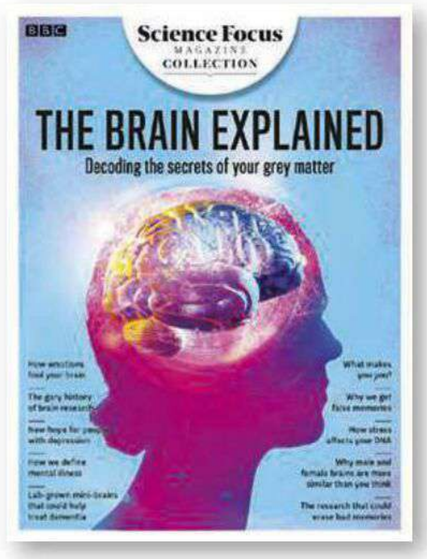
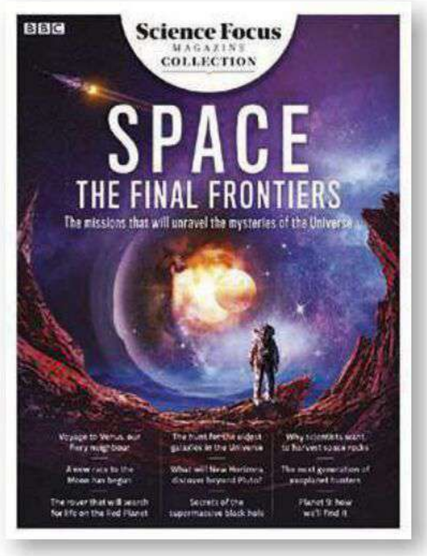
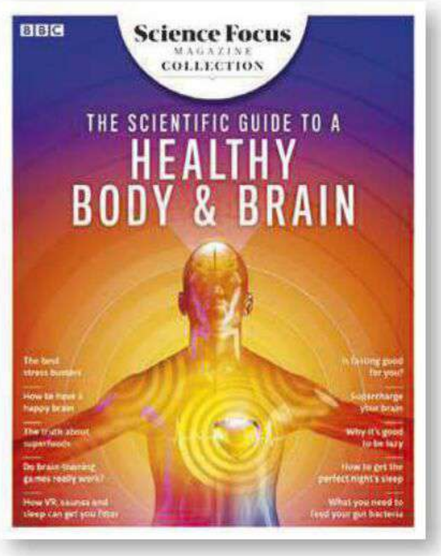


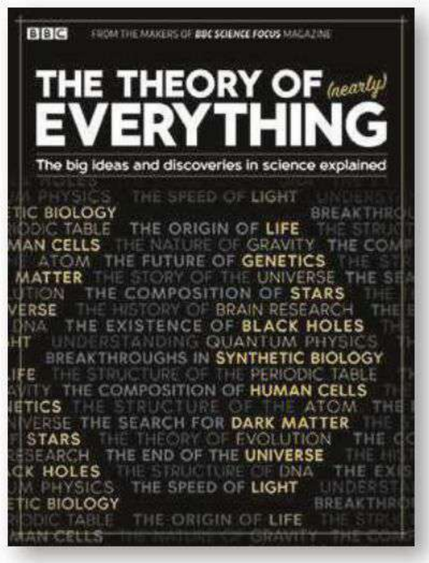
Find out about the extraordinary abilities of the brain, the evolution of intelligence and the latest research into mental health.



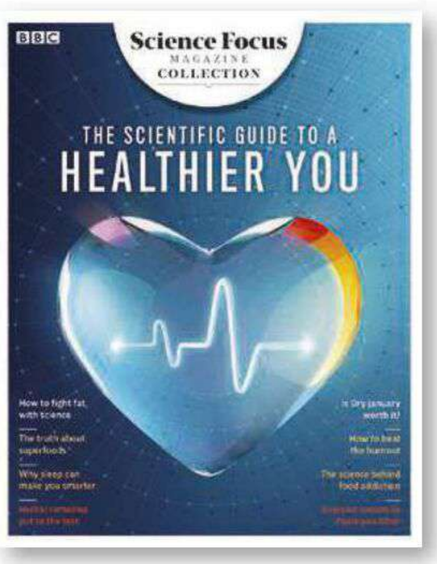
Discover more about the missions that will help unravel the mysteries of the cosmos, from our closest neighbours to the galaxies far, far away.



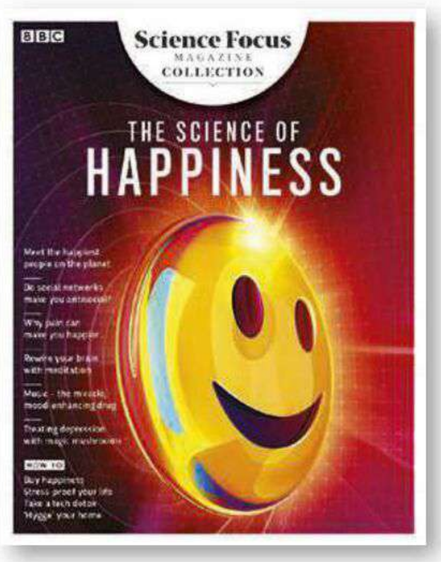
Allow science to show you the best ways to keep your brain sharp and your waistline slim, while staying fit, healthy and happy.



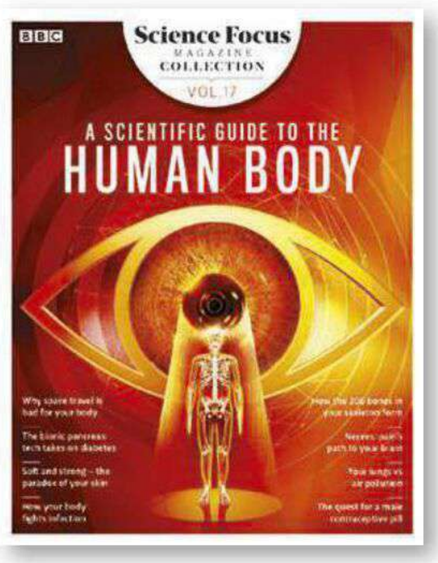
This special issue explains the fundamental concepts of science, and reveals the latest cutting-edge research that will change our world.



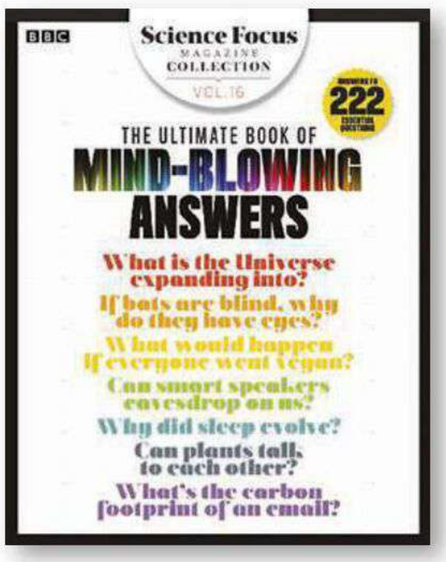
Experts reveal the science behind what really works when it comes to losing weight, eating right, keeping fit and sleeping well.



Brighten up your day with the help of science! Discover the best ways to reduce the stress of daily life and improve your mental wellbeing.



Take a guided tour of the systems in your body that pump your blood, digest your food, fight off infection and deal with pain.



Truth is often stranger than fiction, as the 222 mind-blowing answers to what seem like simple questions demonstrate in this edition.

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THE FUTURE IS FUNGAL

Mushrooms aren't just a delicious pizza topping. They could help us colonise other planets, tackle plastic pollution and even rescue beleaguered bees

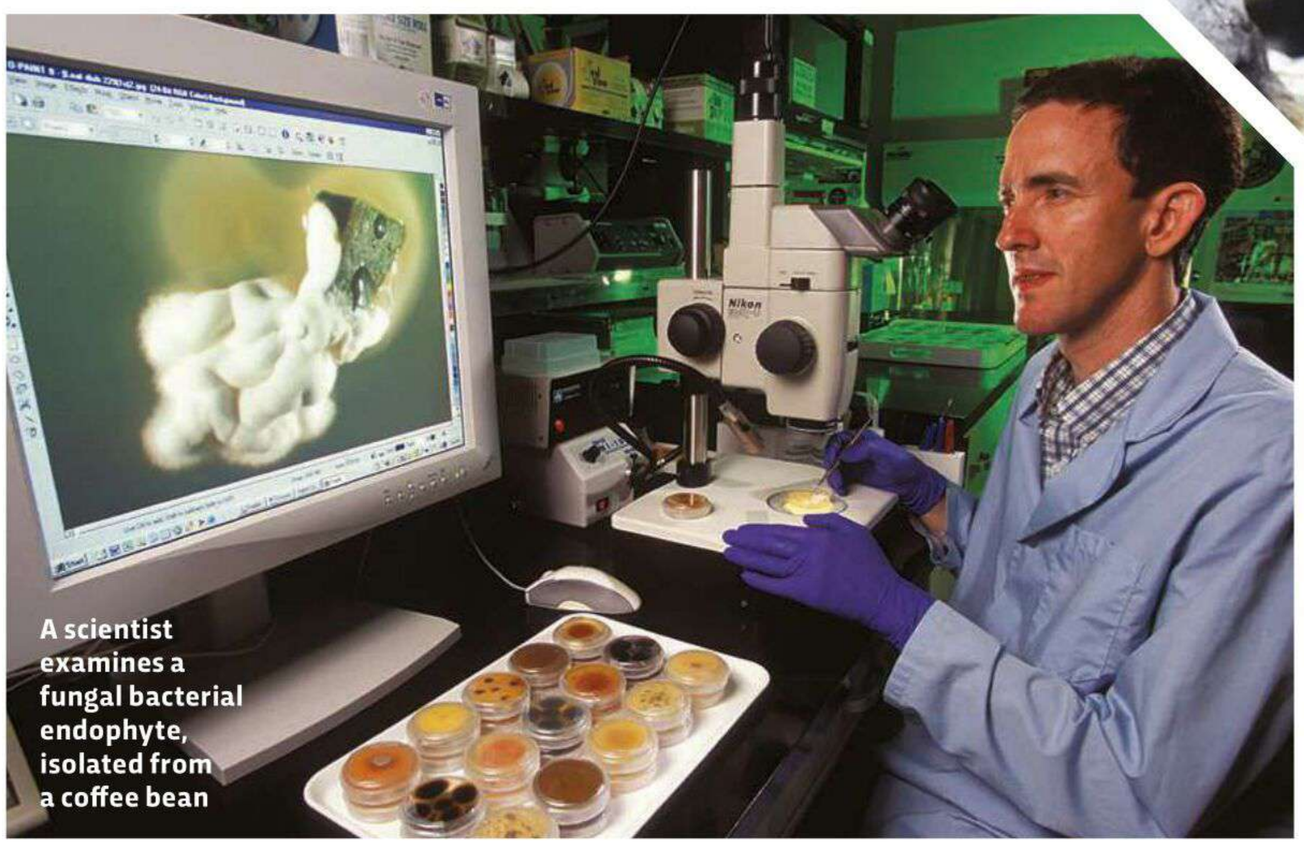
by EUGENIA BONE

Did you know there are 10 times more species of fungi than plants? That with every woodland footfall we are stepping on kilometres of fungal threads? Or that with every breath, we breathe in up to 10 fungal spores? If you don't, you are not alone.

Most of us are ignorant about the fungi kingdom. Perhaps it's because, for many people, these incredible organisms have the 'ick factor'. A large number of fungi are decomposers: they get their food by harvesting nutrients from dead and dying organisms, and we often associate anything to do with decay as rather creepy. What's more, toadstools have been credited with all kinds of mischief, from deflowering virgins (not possible) to melting your liver in a matter of days (very possible, if you eat certain species). Nor has it helped that fungi are primarily microscopic. When we see mushrooms growing in the wild, we are only seeing the fruiting body of the organism, which produces spores for reproduction. The rest of it is a mass of fungal threads called 'hyphae', which are hidden from sight and forage for nutrients inside wood or soil. It wasn't until we had powerful microscopes to see fungi clearly that we were able to understand their metabolism and finally get a sense of how huge the realm of fungi really is.

Fungi are present in the microbiomes of all living things and even exist in the atmosphere. But they mainly reside in soil and plants, where they are integral to the wellbeing of forest and field ecosystems, to the recycling of nutrients, and to the sequestration of carbon. Fungi are responsible for countless duties in nature, and the molecules they have evolved to fulfil those duties represent a range of opportunities that may help us solve some of the world's most vexing problems. This is an exciting time, when bioprospectors, entrepreneurs and ecologists are all rethinking what the future could look like. And what they are seeing is that the future is fungal.

GETTY IMAGES



A scientist examines a fungal bacterial endophyte, isolated from a coffee bean

How fungi could save agriculture in a warming world

You probably don't know it, but when you look at a plant, you are looking at fungi, too. That's because most, if not all, terrestrial plants host thread-like fungi between their cells. The fungi feast on sugars the plant makes, and in exchange, they help plants tolerate stressful environmental conditions like salt inundation, drought and high temperatures. When a plant is exposed to drought it suffers from oxidative stress – an imbalance of free radicals and antioxidants – which can hurt its cells. But unlike you and me, plants don't produce helpful chemicals to counter the effects of that stress; instead, it's the endophytic fungi living between the cells of the plants that do. These impossibly thin fungal threads emit an arsenal of compounds that calm oxidative stress in plants, and also participate in the chemistry that makes plants use water efficiently. This helps plants with a drought problem, but also those suffering from extreme heat or salt exposure.

Researchers have found that stress-reducing endophytic fungi can be transferred from their host plants to crop plants in order to help them survive in a warming world. For example, the fungus that allows panic grass to grow in soil temperatures of up to 65°C also allows tomatoes to grow and fruit in similarly hot conditions. To the fungus, panic grass and tomatoes are the same thing, and the implications are enormous: in a rapidly warming world, endophytic fungi have the potential to protect our food supply.

HOW FUNGI COULD TRANSFORM MIND MEDICINE

There hasn't been a novel psychiatric medicine in decades. The majority of medications used today are next-generation versions of drugs developed in the 1950s. But in the last 15 years, an old class of drugs is new again, and one of the most promising of these is derived from a mushroom.

Fifty years ago, researchers worldwide began an intense investigation into the possibilities of psilocybin and LSD to help people with a range of mental disorders. The research was incredibly promising, but as these drugs seeped into the rowdy, anti-establishment youth culture of the 1960s, fewer and fewer scientists were willing to work with them. By 1968, the United Nations was urging countries to prohibit psilocybin and LSD.

But times change, rigid positions soften, and today those drugs are being researched again, with astonishing results. Researchers have found that when combined with therapy, psilocybin – a molecule present in some 200 species of the *Psilocybe* mushroom genus – may be effective at easing a host of disorders, including OCD, PTSD, depression, and anxiety due to life-threatening illness. There are also ongoing studies to investigate its effect on anorexia nervosa and Alzheimer's.

ABOVE 'Magic' mushrooms like these contain hallucinogens that could be used to help treat mentai illness

SCIENCE PHOTO LIBRARY, GETTY IMAGES, MYCO/STANFORD BROWN, RISD/NASA, WWW.KROWN.BIO

Psilocybin may work by suppressing certain neural pathways in the brain and engaging others, and in the process, it disrupts rigid patterns of thought, as in the PTSD patient who replays traumatic experiences over and over. Psilocybin seems to lead to the rapid onset of antidepressant and anti-addictive effects that are persistent over time. With results like these, governments are paying attention. And so are patients.

WARNING

LSD and psilocybin are Class A drugs according to UK law. Anyone caught in possession of such substances could face up to seven years in prison, an unlimited fine, or both.

Information and support for those affected by substance abuse can be found at **bit.ly/drug_support**

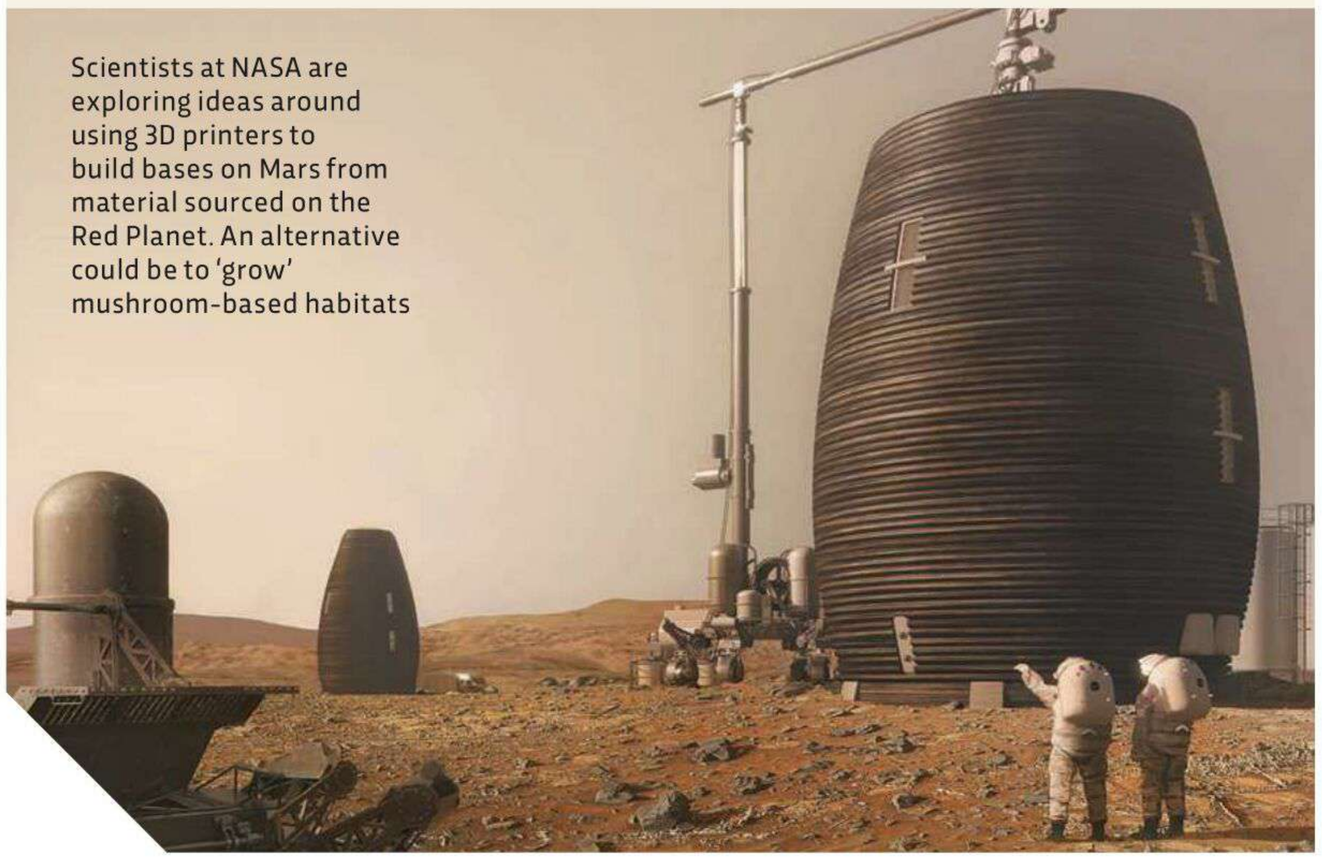
HOW FUNGI COULD REVOLUTIONISE BUILDING AND PRODUCT DESIGN

Take something as simple as polystyrene packing chips. We use them for keeping valuables safe during shipping, but they don't biodegrade. But what if we replaced them with fungal chips? They're just as good at protecting Mum's china and you can toss them into the compost bin when you're finished. Fungi have enormous potential as an environmentally sustainable material for product design and building components. That potential is based on the fact that you can grow mycelium – the non-fruiting part of the fungus, consisting of a network of fine threads – into any shape or size you want, then bake it like a pot in a kiln. The result is a strong, light material that has structural integrity, but as soft or rigid as you like. What's more, the food source used to grow the fungus can lend particular attributes to the end product, like adding fire resistance.

The first company to explore fungi as a material was Ecovative in the US. They have produced a

range of products, from packaging for companies like Dell computers to pleather-like textiles for fashion designers like Stella McCartney. And that's just the beginning. Fungi have also been grown into soft foam alternatives, bricks, particleboard, electrical circuit boards, fire-resistant insulation, and household objects like vases, chairs, lampshades, even slippers.

But why think so small? At NASA's Ames Research Center in California's Silicon Valley, the myco-architecture project is working on technologies that could 'grow' fungi-based habitats on moons and other planets. When it comes to fungi, technology is mushrooming.



Scientists at NASA are exploring ideas around using 3D printers to build bases on Mars from material sourced on the Red Planet. An alternative could be to 'grow' mushroom-based habitats

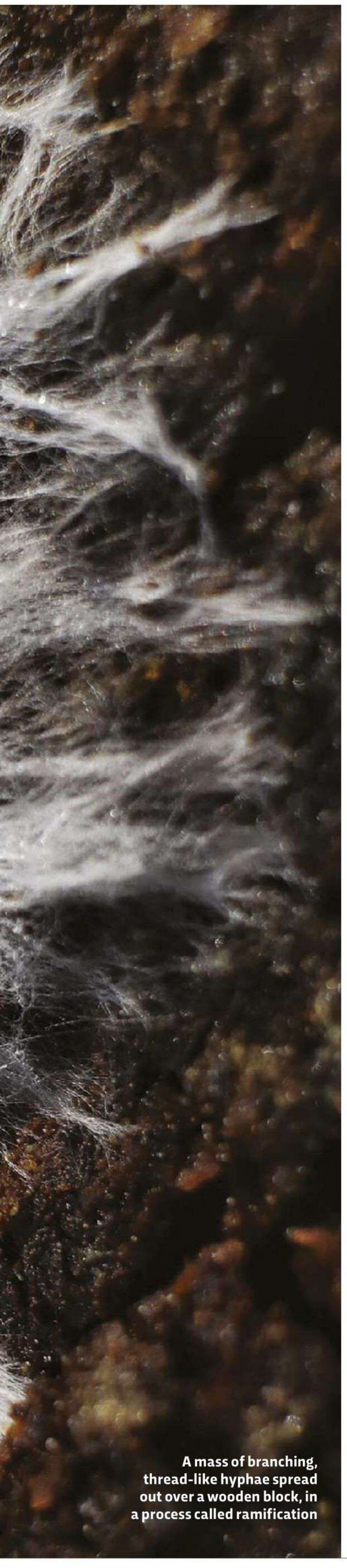
HOW FUNGI COULD CLEAN UP OUR PLANET

Fungi don't have chlorophyll like plants, so to get nutrients, they spread their long, thin hyphae through their food. Their cells will then seep out digestive enzymes, which break down the bonds that hold together their food, allowing them to absorb tasty molecules, like carbon, phosphorous, nitrogen and water. This power to break down complex molecules into simpler ones is the key to mycoremediation, the application of fungi in order to clean polluted sites.

They can be employed in all kinds of ways, from the disassembly of polyaromatic hydrocarbons (think petroleum byproducts, sewage sludge and ash) to an array of nitroaromatic compounds like explosives, dyes, herbicides and insecticides, to ashtrays made of fungi that digest cigarette butts. Basically, any carbon-based product is food for fungi. Fungi have co-evolved with natural materials so they know how to break them down, and now they are learning to do the same for plastics. In the last few years, researchers have identified a soil fungus that can break down polyurethane in a matter of weeks, and other species have been discovered with similar capabilities.

Applying these fungi in situ, and in a cost-effective way, is challenging. But there are exciting new approaches. Researchers in Canada have discovered a fungus living within the roots of dandelions growing on waste products on Canada's Athabasca oil sands. When this fungus was introduced to other plants, it endowed them with its superpower, allowing them to exist on the polluted soil, but also clean it in the process.

Other innovations involve downstreaming industries, like the Onion Collective in Somerset. This biorecycling facility hopes to feed fungi with plastics and make useful products like leather replacement materials with the resulting mycelium.



A mass of branching, thread-like hyphae spread out over a wooden block, in a process called ramification

ALAMY X2, GETTY IMAGES X2, WILD WONDERS OF EUROPE / WOTHE/NATUREPL.COM

How fungi could save the bees

Honeybee pollination is important for many of our crops. But bee populations are in decline all over the world; in China, farmers have been forced to pollinate their apple trees by hand. This decline is credited to Colony Collapse Disorder (CCD), characterised by the sudden death or disappearance of worker bees in a hive. Widespread in the US, Canada and Europe, CCD kills billions of bees each year. Why? One theory posits the bees' immune systems are compromised by exposure to neonicotinoid pesticides. As a result, they can't fight viruses spread by a parasitic hive mite. And that's where mushrooms might come in.

In the mid-1980s, the mycologist and mushroom supplement producer Paul Stamets noticed that his honeybees were sipping droplets of liquid emitted by mushroom mycelium that had colonised a pile of wood chips. For years, he assumed the bees were collecting sugar. And then it occurred to him, maybe the bees were collecting medicine. That concept was borne out in 2018 when Stamets, along with researchers at Washington State University, found that honeybees fed an extract from tinder fungus (*Fomes fomentarius*) and reishi mushroom (*Ganoderma lucidum*) experienced a significant reduction in their viral load, particularly the lethal deformed-wing virus. The researchers are not sure yet whether the extracts are helping the bees' natural immune system fight off the virus or actually destroying the virus, but future studies will tell. We may soon be putting out medicinal dispensaries for bees along with our bird feeders. **SF**

ABOVE Studies show that feeding honeybees an extract from tinder fungus (above left) and reishi mushroom (above) resulted in a reduction in the lethal deformed-wing virus

by **EUGENIA BONE**

Eugenia is a food and nature journalist and author of six books including Mycophilia: Revelations From The Weird World Of Mushrooms. *She is featured in the documentary* Fantastic Fungi *with Paul Stamets and Michael Pollan.*

COOKING UP ALIEN ATMOSPHERES

Scientists are recreating the air that clings to distant worlds. Could their work help to reveal the presence of extraterrestrial life?

by PHILIP BALL

How do you spot an alien? Some scientists are looking for communication signals beamed out into space. Others propose looking for dips in starlight that might be caused by huge alien-built megastructures orbiting a distant sun.

But perhaps the most promising line of enquiry lies with probing the layer of gases surrounding alien worlds. If we were to watch Earth from afar, we would be able to infer our existence by analysing the make-up of our atmosphere. There's only one process we know of that could keep it so rich in oxygen: life.

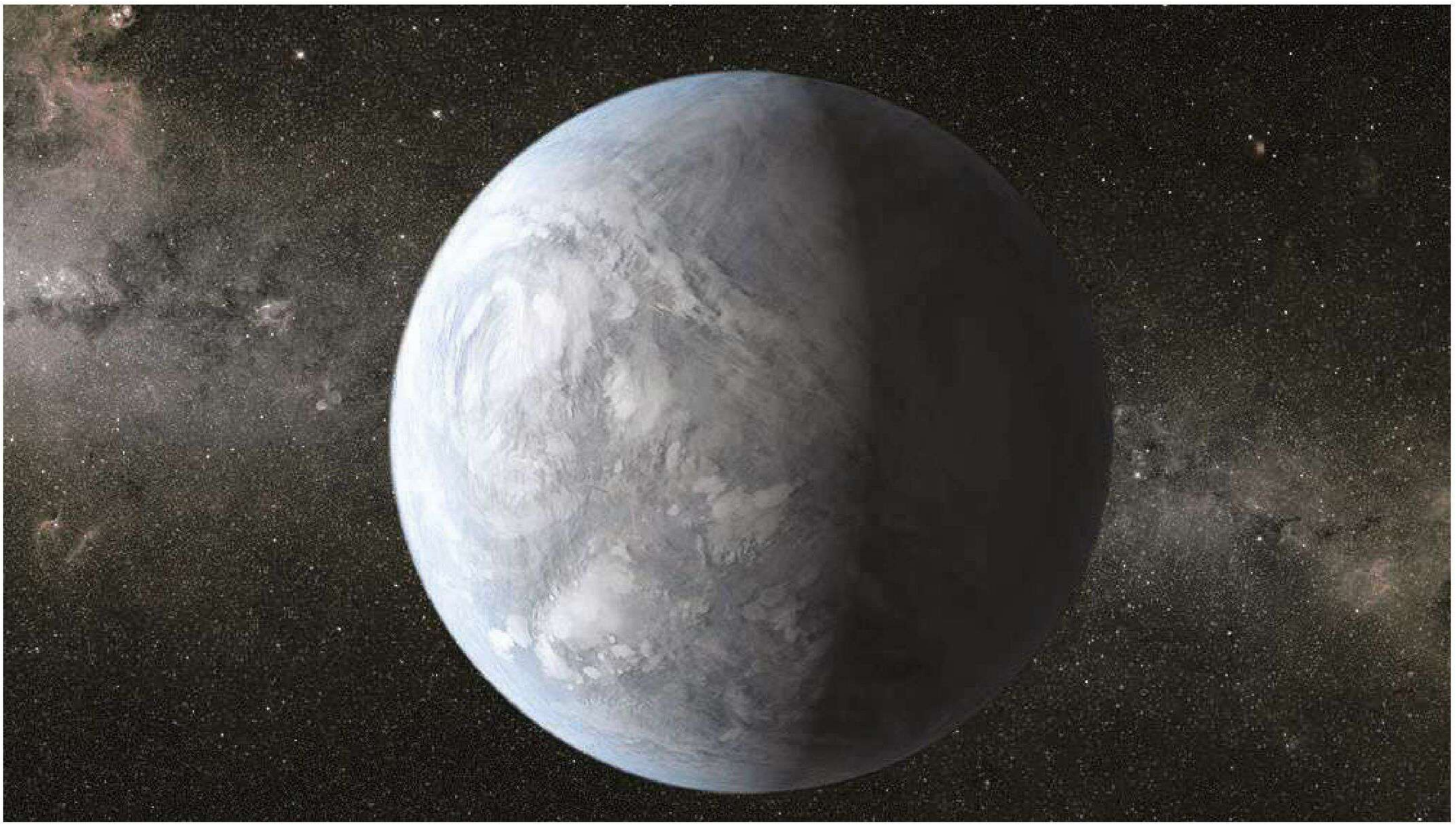
If aliens live on other worlds, they'd probably also imprint a signature of their existence in their atmospheres. While we are able to peer at alien atmospheres through the latest space telescopes, there's a catch: we don't really know what we're looking for. We only have Earth as a comparison – but what if there are other combinations of gases that can reveal the presence of life?

The answer to this question may lie in intriguing new research that's replicating alien air on Earth, cooking up exotic brews in laboratories. Meanwhile, other scientists are simulating the weather and circulation of alien atmospheres inside powerful supercomputers to find out just how hospitable distant worlds may be. This research is already providing some tantalising clues about where the next generation of alien hunters should be focusing their attention.

GETTY IMAGES

SOMETHING IN THE AIR

Since the first detection of an exoplanet – a planet around another star – in 1992, more than 4,000 have been identified, mostly by observing the subtle but regular dimming in starlight as the planet passes across its parent star and blocks some of its light (a transit). More than half ➲



of exoplanets were detected in this way by NASA's Kepler space telescope (active from 2009 to October 2018). In April 2018, NASA launched a successor to Kepler: the Transiting Exoplanet Survey Satellite (TESS).

In order to study an exoplanet's atmosphere, astronomers look at how the atmosphere absorbs the starlight passing through it. Different molecules of gas will absorb different wavelengths of light, so researchers can analyse the star's filtered light spectrum during a transit to pin down which gases are present. In this way, astronomers made the first direct detection and chemical analysis of an exoplanet atmosphere in 2001 – finding sodium in the atmosphere of a gas giant known as HD 209458 b.

Since then, several exoplanets have had their atmospheres analysed, revealing the presence of water vapour, methane, carbon dioxide and even small amounts of oxygen around some of these worlds. None of these gases alone signals life, however – not even oxygen, as we know of processes that can create small amounts of it without involving living organisms.

This is where the work of planetary scientist Dr Sarah Hörst comes in. At Johns Hopkins University in Baltimore, US, she is leading a team of scientists who are brewing lab simulations of the gases likely to be in exoplanet atmospheres, in order to find out what they might produce. So far, Hörst's work has focused on an atmospheric phenomenon that'll be familiar to anyone who's spent time in a big city: haze.

COOKING WITH GAS

The two most common types of exoplanet have no equivalent in our own Solar System. One is the 'super-Earth': rocky, with a diameter 1.25 to two times that of Earth. The other is the 'mini-Neptune': about two to four times the size of our planet, with a thick blanket of gases (mostly hydrogen and helium) over a dense core of rock or ice.

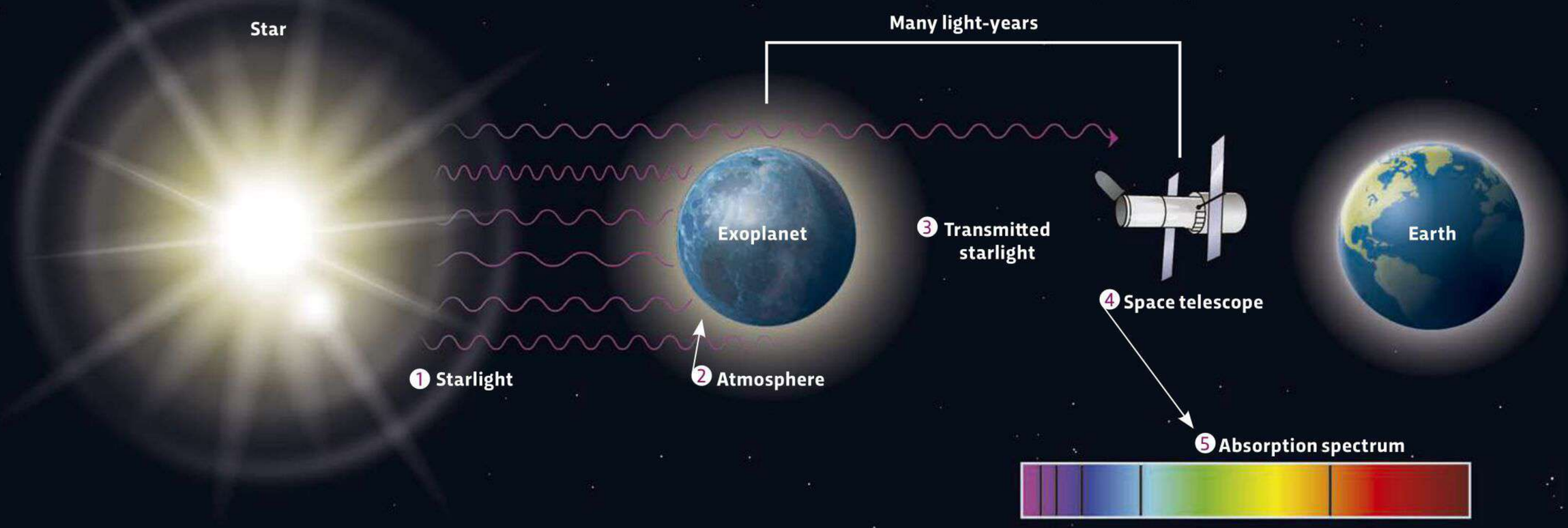
Astronomers have discovered that the atmospheres of super-Earths and mini-Neptunes are rather thick and misty: light doesn't get through them easily. This could be because they're full of clouds (perhaps made from droplets condensed from water vapour or other gases such as methane), or it might be due to haze: tiny, dust-like solid particles, like the pall over cities caused by traffic fumes. Hörst is trying to find out. She says that there might be ramifications for whether planets like this could support life. According to Hörst, haze particles in an atmosphere can have a huge impact on how starlight moves through it. "This can affect things like how much and what sort of energy is available at the surface of a planet for life, and what the temperature of the surface is," she says.

We have only the sketchiest information about the chemistry of these atmospheres, so Hörst carries out simulations for a wide range of possible compositions, including all the common gases likely to be found around worlds like these: water vapour, carbon monoxide, carbon dioxide, nitrogen, hydrogen, helium and methane. Hörst mixes up

ABOVE Super-Earths like Kepler 62e are a common type of exoplanet, with thick and misty atmospheres

RIGHT Dr Sarah Hörst and assistant research scientist Chao He examine a sample of simulated exoplanet atmosphere

HOW TO ANALYSE AN ALIEN ATMOSPHERE



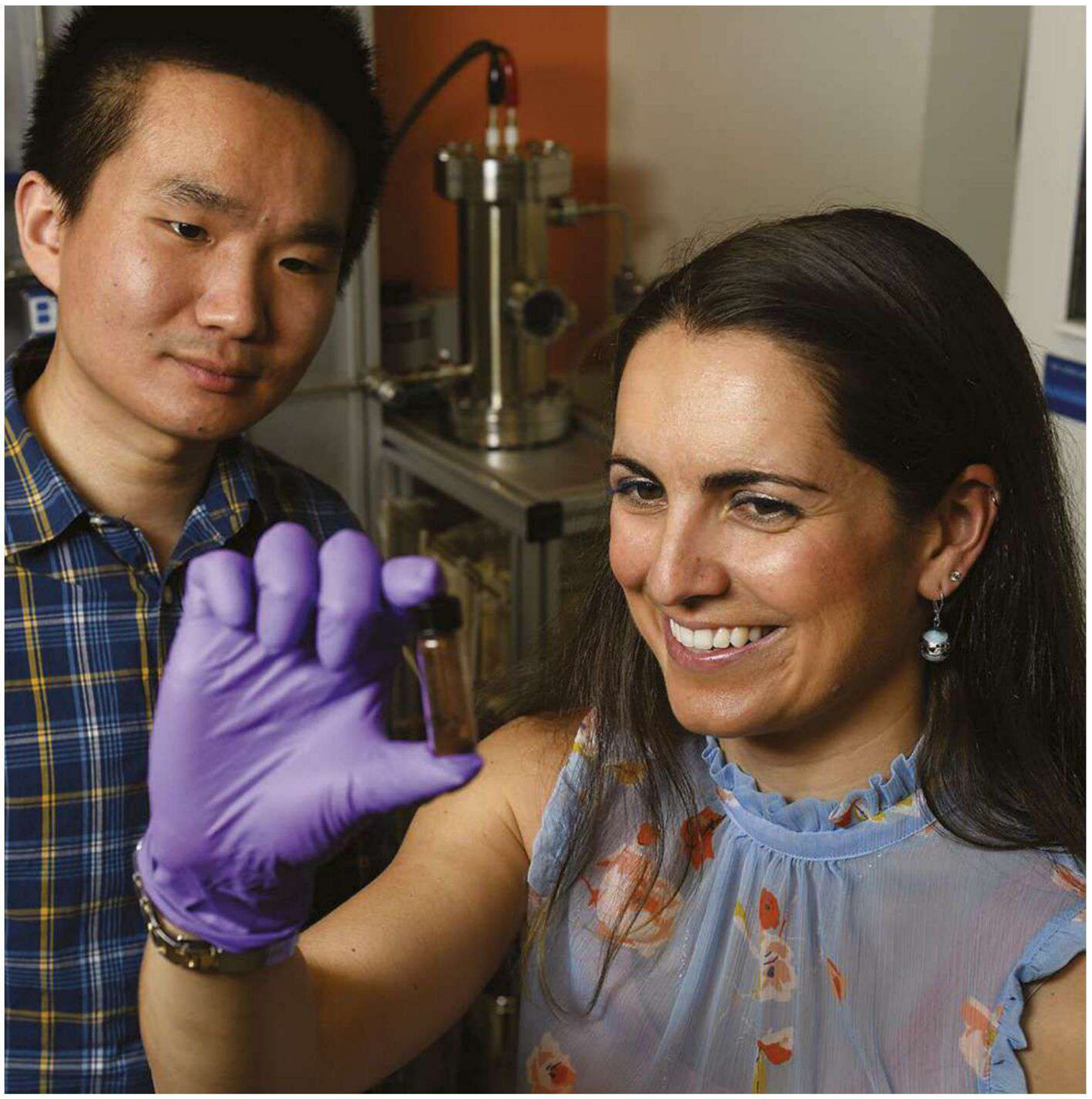
1 The star's light is made up of many individual wavelengths

2 The starlight passes through the exoplanet's atmosphere

3 The atmosphere absorbs specific wavelengths of starlight, depending on which gas molecules are present – leaving a 'fingerprint' of those molecules in the transmitted light

4 During the exoplanet's 'transit' across its star, a space telescope such as Hubble – or soon the James Webb Space Telescope – detects the filtered light and analyses its spectrum using a device called a spectrograph

5 Gaps in the star's spectrum indicate the presence of particular gas molecules in the planet's atmosphere



NASA, WILL KIRK/JHU ILLUSTRATION: ACUTE GRAPHICS

different proportions of these gases at temperatures between about 25°C and 325°C, mimicking the conditions thought to exist on super-Earths and mini-Neptunes.

It's a kind of cosmic cookery: throw together the ingredients, bake at moderate heat, and see what comes out. There's another crucial ingredient, too: energy to kick off chemical reactions by breaking molecules apart. On exoplanets, this could come from high-energy ultraviolet rays in the starlight, or from electrically charged particles formed by cosmic rays flooding into the upper regions of the atmosphere. The researchers simulate these energy sources using either an ultraviolet lamp or an electrical discharge like that in a fluorescent lighting tube.

Most of the mixtures that Hörst and her team have studied generated brownish, smog-like haze, similar to what we see on Saturn's moon Titan. The amount of haze varied widely, though, depending on the composition of the mixture. For example, two of the experiments with plenty of water vapour and methane produced the most haze, but a third experiment also generated fine particles with no methane present at all.

More work is needed to find out

"IT WON'T BE LONG BEFORE WE'RE ABLE TO STUDY THE ATMOSPHERES OF EVER MORE EXOTIC EXOPLANETS"

what the detection of haze on a distant exoplanet would mean for the likelihood of finding life. Hörst says that in some cases haze might block harmful radiation (as the ozone layer does on Earth), but it could also lead to cooling of the surface and a lack of liquid water. "We need to know more about the planet and its atmosphere to be able to understand what the conditions might be like on the surface, and what processes would have led to the formation of haze," she says.

In the meantime, the holy grail of this area of research is to identify some molecule – or a set of molecules – that can exist only if there is life, i.e. a 'biosignature' of alien life. But what might that be?

The answer doesn't appear to be oxygen alone. Hörst and colleagues saw oxygen form in their simulation experiments, purely from chemical reactions induced by ultraviolet light. They also saw organic molecules like ethanol and formaldehyde, which rules these out as definite biosignatures, too. One possible biosignature is the simultaneous existence of ozone and methane, says Hörst. This is a chemically unstable blend of gases, and there's no known geological process that could sustain them. "It would be really hard to have them together in the same atmosphere without some source replenishing them," says Hörst. On Earth, the biosphere is ultimately the source of both of these gases in our atmosphere.

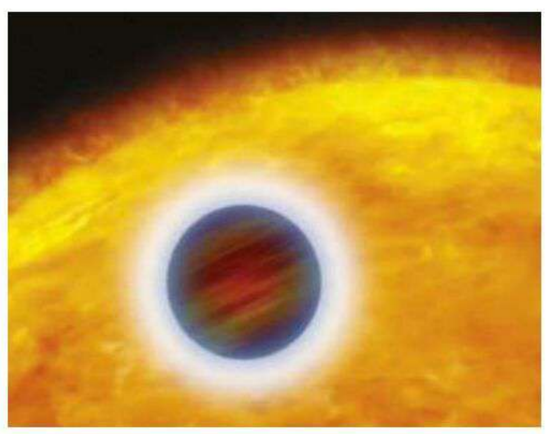
Some of the most enticing worlds to look for biosignatures such as these, Hörst feels, are the set of planets detected in 2015 around a dim star called TRAPPIST-1, located 40 light-years away in the constellation of Aquarius. Seven of the worlds orbiting this star are vaguely Earth-like, and most of them are potentially habitable, having the right conditions for liquid

WEIRD WEATHER

Think Earth's weather is unpredictable? Here are some of the strange phenomena we've spotted elsewhere in the Universe

DIAMOND RAIN

The atmospheres of some gas giants contain plenty of carbon, created when lightning reacts with methane. At high pressures and temperatures inside the atmosphere, this might condense into crystals of diamond, some as big as blueberries. Experts estimate that, on Saturn, about 1,000 tonnes of diamonds are produced every year.



METAL MONSOON

The hot Jupiter HD 209458 b, also known as 'Osiris', has atmospheric temperatures of several thousand degrees. It's likely that rains of molten iron or silicate glass pelt down there, falling in wind speeds of several kilometres per second (compared to a mere 70 metres per second for severe hurricanes on Earth). The result is a lacerating blast of hot metal and rock.

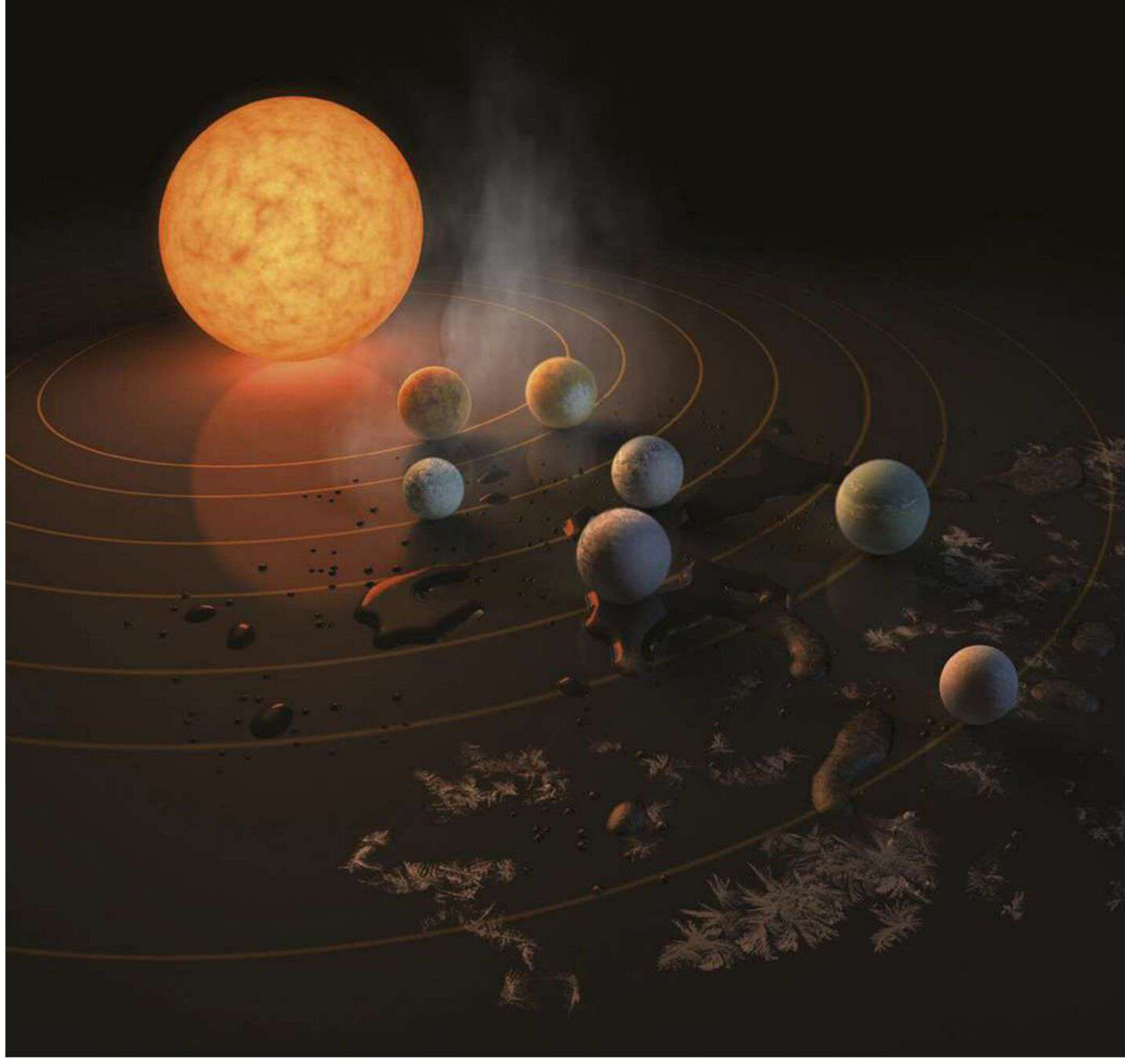
INFERNAL STORM

55 Cancri e is a rocky planet about twice the diameter of the Earth that orbits so close to its star that its surface has a temperature of around 2,000°C. Molten lava spouts into the atmosphere to fall as fiery rain, and this turbulent, sooty atmosphere is filled with electrically charged particles, producing immense, planet-wide lightning storms.

GEMSTONE CLOUDS

HAT-P-7b, a hot Jupiter located 1,000 light-years away, has clouds on its cool, night side made of condensed aluminium oxide – the stuff that forms the basis of minerals like rubies and sapphires. Winds carry these clouds to the planet's hot day side, where temperatures of close to 2,000°C quickly destroy them.

NASA/JPL X2, ESA, SCIENCE PHOTO LIBRARY



RIGHT By studying their atmospheres, we can confirm if some of the planets surrounding the TRAPPIST-1 star have the right conditions for liquid water to exist

water on their surfaces. By looking at the light transmitted through their atmospheres, Hörst and coworkers have found that some of them may have clouds or haze, though it's hard to be more precise at this stage about which option is more likely.

Hörst thinks that these intriguing planets should be an early target for NASA's James Webb Space Telescope (JWST), the planned successor to the Hubble Space Telescope, which will take a closer look at exoplanet atmospheres once its been launched in 2021.

EXO-CLIMATES

Life on Earth relies not only on having the right kind of atmosphere, but also on the whole climate system: how air, oceans and heat circulate, and how clouds form. If we found an exoplanet with an identical atmospheric composition to Earth, it might still be inhospitable to life if it lacked a similar climate system. A new research area called 'exoclimatology' is aiming to understand exoplanet climates – and their implications for life – by applying the computer models used to simulate the Earth's weather and climate to other worlds.

So far, much of the work has focused on another common exoplanet type: 'hot Jupiters' – gas giants like our own Jupiter but which orbit much closer to their parent star. They tend to either rotate very slowly or be 'tidally locked' so that – as with the Moon orbiting the Earth – the same side always faces the star. This gives the planets a temperature difference between the 'day' side and the 'night' side which drives atmospheric circulation, much as the temperature difference between Earth's equator and the poles powers our own climate.

Computer models of this circulation indicate that hot Jupiters have a kind of atmospheric jet stream, says Dr Nathan Mayne, who leads the exoclimatology group at the University of Exeter. This can mix up the chemistry of the hot and cool sides of the atmosphere, changing the blend of gases in some places and thus the amount of starlight that's transmitted to the surface. While hot Jupiters are not likely to harbour life, this shows how the circulation of the atmosphere can play a crucial role in the surface conditions on a planet – with important implications for their habitability.

Add water to the equation and things get even more interesting. Some potentially habitable planets like the TRAPPIST-1 group are also likely to be tidally locked to their star. If these exoplanets have liquid water on their surface, then water on the hot day side will evaporate, eventually condensing into rain or snow on the cooler night side. "Land covering the day side would quickly dry out and the moisture would be transported to the night side," says Mayne. "But if there's an ocean, the water can circulate back" – creating a giant conveyor belt of water between the two sides of the planet. This could make the difference between a barren planet divided into halves – each too extreme for life to exist – and a planet where water circulation creates a more moist and clement environment.

With the latest generation of space telescopes, it won't be long before we're able to study the atmospheres of ever more exotic exoplanets. "The combination of TESS and the JWST should provide us with a lot of compelling worlds to study," says Hörst. Work by the likes of her and Mayne is set to become crucial to astronomers who want to know whether the exoplanet gases and weather patterns that they're detecting are the symptoms of a sterile planet, or maybe – just maybe – hints of life... **SF**

by **PHILIP BALL**

Philip is a freelance science writer, specialising in physics and maths

DISCOVER MORE

LISTEN

In this episode of The Curious Cases Of Rutherford & Fry, *find out if we'll ever discover alien life.*

bit.ly/find_alien_life

HOW TO GROW FOOD IN SPACE

TO DEVELOP WAYS TO FARM ON OTHER WORLDS, GREEN-FINGERED SCIENTISTS ARE HEADING TO ANTARCTICA. HERE, THE BLEAK, COLD AND REMOTE CONDITIONS PROVIDE SIMILAR CONDITIONS TO SPACE

WORDS: **HAYLEY BENNETT** PHOTOGRAPHY: **ESTHER HORVATH**

Today's astronauts have to exist largely on pre-packed meals, with fresh fruit and veg being a rare treat. But indoor farming technologies are advancing, and the race is on to find effective ways to grow food in space – both for long-duration missions, and for future settlements on the Moon or Mars. So where's the best place to test these technologies? The bottom of the world, it turns out. At the Alfred Wegener Institute's Neumayer III station in Antarctica – a German base for polar research – scientists have created a standalone greenhouse as part of a project called EDEN ISS, which develops food production techniques for the International Space Station (ISS) and future human space colonies. Here, researchers are already seeing the fruits, or at least vegetables, of their labour.

FROZEN VEG

The frozen landscape of Antarctica might seem an unlikely place for a greenhouse, but the isolation, limited resources and harsh environment make it an ideal analogue of the conditions faced by astronauts growing crops in space. The 12-metre-long mobile facility – made from two interconnected shipping containers – houses soilless technology for indoor farming, including temperature and humidity control systems, water recycling, automated nutrient pumping, LED lighting and remote plant monitoring. It was kitted out in Germany and shipped to Antarctica in October 2017.

In this picture, EDEN ISS leader Dr Daniel Schubert (right) and a colleague drag a sledge loaded with supplies to the greenhouse facility, which is about 400 metres from the main Neumayer III station. It's "a pain in the ass" to get to in these conditions, Schubert says, explaining that the greenhouse is positioned this far away because of the huge snowhills that form behind any large object. The main station itself avoids this problem because it is specially shaped and raised on hydraulic stilts to prevent snow from accumulating.

PUTTING DOWN ROOTS

The cultivation process at EDEN ISS is aeroponic – a soilless system where the crops absorb nutrients from a water mist applied at the roots. The vegetables are grown in vertical racks, giving a total growing area in the greenhouse of 12.5 square metres, with the roots exposed in plant growth trays.

Everything in the greenhouse can be regulated remotely from mission control at the German Aerospace Centre in Bremen, except, notes Schubert, seeding, harvesting and cleaning up – these have to be done by hand. Here, horticultural engineer Markus Dorn (right) prepares the seed trays using blocks of rock wool soaked in nutrient solution. Rock wool, which is made by spinning molten rock into fibre, has a candyfloss-like texture that holds onto water and helps stabilise roots. The seeds will germinate in the seed trays for about two weeks before being transferred to the vertical racks.

↑

UNDER SURVEILLANCE

The greenhouse features a crop surveillance system: high-definition cameras that help the team keep tabs on the plant growth trays. In this image, plant scientist Dr Anna-Lisa Paul from the University of Florida is calibrating a specially adapted camera that is capable of detecting crop stress – in kohlrabi, in this case – even before it's visible to the eye. (The colour plate helps to make sure the colours are aligned between different images.) Healthy, unstressed plants that are well-hydrated and have all the right nutrients reflect a higher ratio of light in the 'near-infrared' part of the spectrum compared to shorter wavelength blue and green light. The camera is able to detect these wavelengths, determining whether the plants are stressed or healthy. Paul says that this means problems can be addressed before they become irrecoverable. "This is especially important when resources are limited, and the habitat is inherently challenging, such as in space," she says.

→

REAP WHAT YOU SOW

Over the 2018 Antarctic winter, between February and November, the greenhouse produced 268 kilograms of crops, including 67 kilograms of cucumbers and 50 kilograms of tomatoes. The impressive harvest shown here was collected early the following year, in January 2019. In addition to cucumbers and tomatoes, the crew were treated to swiss chard, radishes, fresh herbs and different varieties of lettuce. The LED lighting is tuned to produce mostly red light, as this is the most effective colour for driving photosynthesis, but there are seven different light 'regimes' tailored to the height of the crops and the amount of light they need. "We've developed specific light mixtures for the plants," says Schubert. "So the lettuce, say, receives a different light mix than the cucumbers." The light also scales up slowly in the morning, creating an artificial dawn. Except for tomatoes, no fruit is grown here, but the crew members have frozen fruit in their stores.


L1-2R
L2-1L
L12-1S
L2-2L

FRESHLY CUT

With no hair salons for thousands of kilometres, station leader Dr Bernhard Gropp has taken up the clippers, giving electrical engineer Thomas Schad a haircut. Team bonding is important in these extreme conditions. In winter the temperature can fall below -40°C, and the polar night means that for 11 weeks of the year no sunlight touches the ice. As in space, a haircut and a few fresh greens might provide the crew with a boost in morale. The psychological impact of the fresh produce at Neumayer III is the subject of ongoing research. "We have a dedicated research team that's evaluating this with questionnaires and group discussions," says Schubert. "It seems like there is a positive effect." The EDEN ISS project is set to continue until at least 2021, with plant researchers worldwide being invited to propose studies for this unique facility.

SPLENDID ISOLATION

Every year, the Neumayer III research station, viewed here from the window of one of the Alfred Wegener Institute's helicopters, moves about 150 metres north, along with the Ekström ice shelf on which it sits. It's a lonely place, particularly during the nine-month winter, when nine crew members (three of whom share responsibility for the plants) spend the season completely detached from the outside world. During the summer, the number of scientists at Neumayer III swells to around 50, with multiple projects covering research topics ranging from air chemistry to marine ice to penguins.

Despite the isolation, there is close contact all year round between crew members in Antarctica and colleagues back in Germany. "Nowadays, it's quite easy," says Schubert. "We have a big WhatsApp group with the overwinterers, and a dedicated greenhouse chat group." But while the remote scientists can advise if something goes wrong, on-site technical expertise is crucial, just like in space. **SF**

DISCOVER MORE

BBC RADIO 4 *Listen to the president of the British Antarctic Survey Jane Francis tell Jim Al-Khalili about camping on the ice in Antarctica in this episode of* The Life Scientific ***bit.ly/jane_francis***

by **HAYLEY BENNETT** *(@gingerbreadlady)*
Hayley is a science writer based in Bristol, UK.

HOW TO SMASH AN ASTE

ROID

Next year, a craft will race across space on a suicide mission to smash into a space rock. Why? To help astronomers test the feasibility of deflecting dangerous asteroids that are on a direct collision course towards our planet

by DR STUART CLARK

Remember, the film *Armageddon*? It's the one where Bruce Willis climbs aboard a space shuttle, and uses a nuclear bomb to blow apart an asteroid the size of Texas just hours before it hits Earth and wipes out all life as we know it. Although the film can hardly be described as scientifically accurate, a new mission by NASA and the European Space Agency (ESA), called the Asteroid Impact and Deflection Assessment (AIDA), will attempt to make some of it come true.

In late July 2021, the first part of the mission, NASA's Double Asteroid Redirection Test (DART) will launch from Cape Canaveral on a suicide trip. The spacecraft will set course for the binary asteroid system Didymos, and after a 14-month chase, DART will smash straight into the space rock. The aim is not to shatter the target, but to change its orbital speed by a small amount – the kind of deflection that could save our planet should an incoming asteroid be detected.

AVERTING ARMAGEDDON

The threat from asteroids comes on a number of different scales, none of them good. At the most extreme end are the so-called 'global killers'. These are asteroids larger than 10 kilometres in diameter. As the name suggests, it was an asteroid in this category that wiped out the dinosaurs 65 million years ago.

Thankfully, we don't need to worry too much about a repeat of that cataclysm. "We're 95 per cent sure we are not going to get whacked by a global killer in the next hundred years," says Prof Alan Fitzsimmons, an astronomer at Queen's University Belfast. We know this because planet-killing asteroids are relatively bright due to their size, and have been picked up in surveys over the past few decades. None of them are close enough to cause any sleepless nights at the moment.

GETTY IMAGES, ALAMY, SHUTTERSTOCK

BOTTOM LEFT When the asteroid entered the atmosphere over Chelyabinsk in 2013, it exploded, leaving contrails behind

TOP LEFT The shock wave from the explosion shattered windows and damaged some buildings, like the factory pictured here

ABOVE A large fragment of the asteroid plummeted into Lake Chebarkul, leaving behind an eight-metre hole in the frozen surface

It's a different story at the other end of the scale, where the asteroids are smaller and dimmer. "We've still not found the majority of smaller asteroids," explains Fitzsimmons. "Our catalogues are woefully incomplete at this stage – not through lack of trying but simply through lack of resources."

"We're 95 per cent sure we are not going to get whacked by a global killer in the next hundred years"

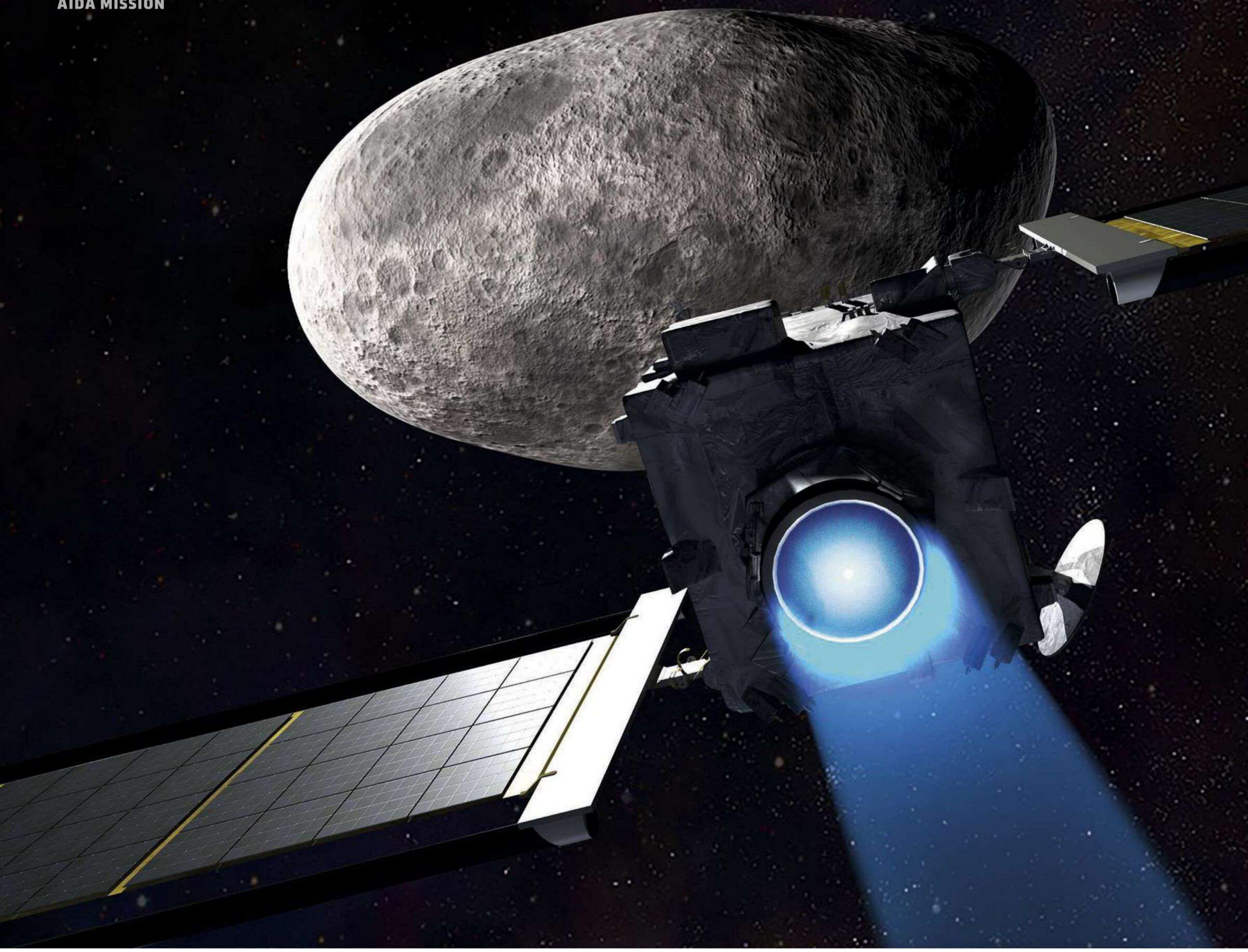
And this is a big concern. Asteroids between 100 and 300 metres across are dubbed 'city killers' because when they hit, they could easily devastate a city. In 1908, an asteroid at the lower end of this size range struck the Earth in the Tunguska region of Siberia, Russia. Thankfully, it was an uninhabited area and no one is thought to have died, but the destruction was astonishing. The impact blast flattened 2,000 square kilometres of forest. Had it taken place over central London, the devastation would have just about stretched to where the M25 is today.

In 2013, a 20-metre asteroid entered the atmosphere over the Russian city of Chelyabinsk. It exploded in mid-air, creating a shock wave that shattered windows across the city, injuring around 1,600 people.

"When one balances the likelihood of impact with how many of those kinds of asteroids are out there, it's likely that the biggest threat to us is from a currently unknown asteroid between 100 and 300 metres across," says Fitzsimmons. "It will lay waste to whatever it hits, and if it's 300 metres across that will be a very large area: about the size of a small state."

The European part of the AIDA mission is called Hera, named after the Greek goddess of the starry heavens. This spacecraft will arrive about three years after DART's impact to study the results of the cosmic smash-up. And as unlikely as it seems, part of the reason it exists is probably down to that glitzy Hollywood blockbuster.

"It was not so long after the film *Armageddon* that people were wondering what the real space agencies would do in that situation," says Ian Carnelli, the manager of ESA's discovery and preparation team, located at ESA's headquarters in Paris. That early round of interest led to ESA putting together a team of experts called NEOMAP, the Near Earth Object Mission Advisory Panel, of which Fitzsimmons was a member. They came together in the early 2000s to assess missions that could address threatening asteroids. They ➤



ABOVE The DART craft is due to arrive at Didymos in 2022, where it will smash into Didymoon

NASA/JOHNS HOPKINS

decided that the best option would be a deflection test like AIDA, but it came at a cost. "It was clear from the very beginning that this was an expensive mission and would require international collaboration," says Carnelli.

PICKING A TARGET

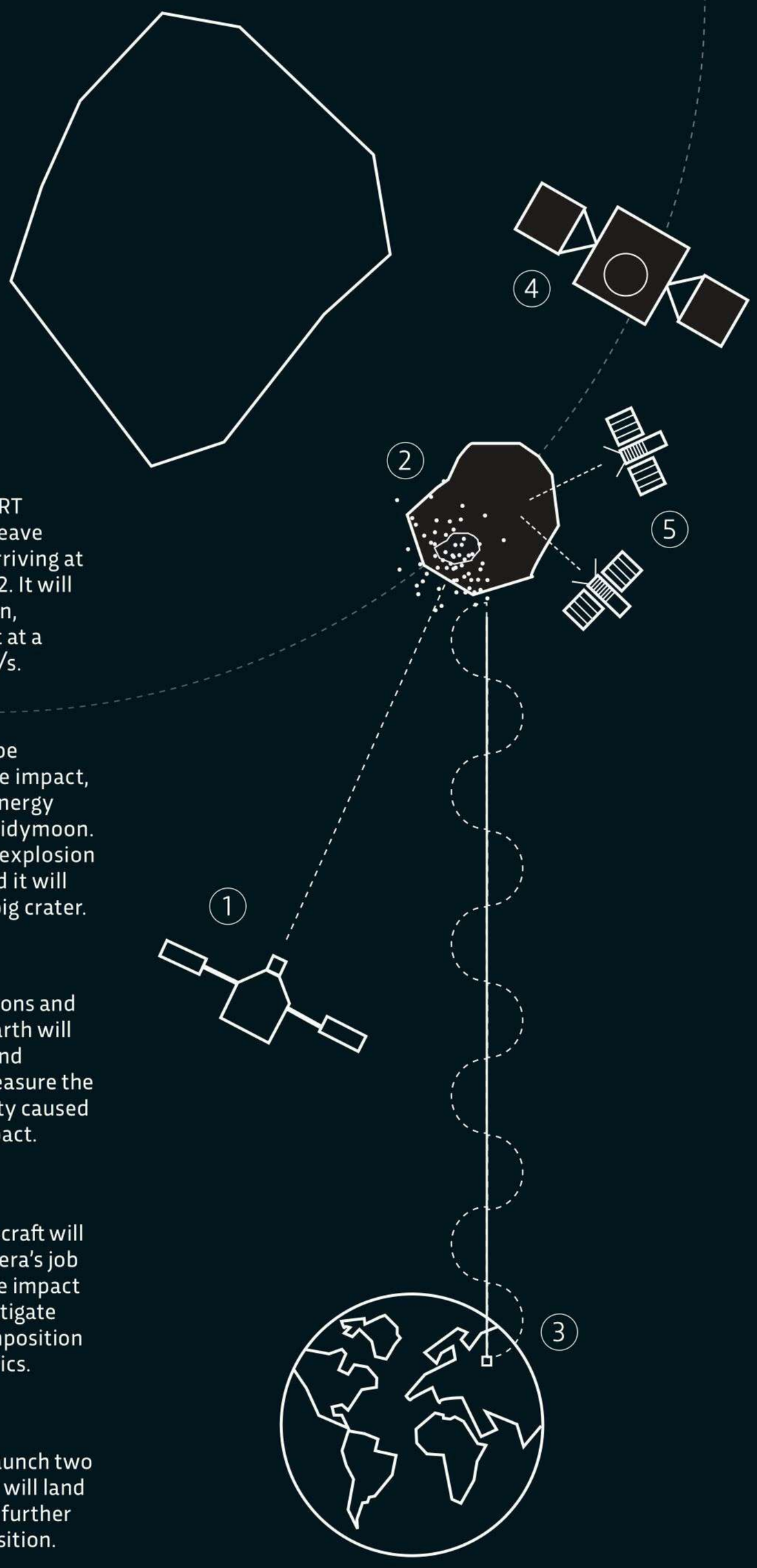
There was another stumbling block to a deflection test: technology. The original mission targeted an asteroid known as 2002 AT4, and would attempt to alter its velocity by around 0.5 millimetres per second. But trying to measure this minuscule change was particularly difficult because the asteroid was travelling around the Sun at 30 to 40 *kilometres* per second. Astronomer Dr Andrew Cheng of Johns Hopkins University came up with a solution. Instead of targeting a single asteroid, he suggested to find a pair that are in orbit around one another and target the smaller of the two. That way the 0.5 millimetres per second will be much easier to measure because the pair will only be moving around each other at a few centimetres per second.

This is where the asteroid Didymos comes in. It was discovered back in 1996, and was shown to be a pair of asteroids in 2003. The largest is 750 metres in diameter, the smallest is 170 metres. Nicknamed Didymoon, the little one is the target for DART because it is in exactly the size range that Fitzsimmons and other experts think is most dangerous to Earth.

The DART mission is a crucial experiment for humankind to conduct for one very good reason. "Unlike any other natural disaster, asteroid and comet impacts are things that we can actually do something about," says Dr Andrew Rivkin of Johns Hopkins University, who leads the DART investigation. He points out that we can take precautions against the damaging effects of other natural disasters, by building earthquake-resistant houses, for example, but

THE AIDA MISSION

Didymos – meaning ‘twins’ in Greek – is a binary asteroid system consisting of two asteroids orbiting each other. The smaller of the two is nicknamed Didymoon. The AIDA mission will smash into Didymoon to change its velocity, to investigate how we could deflect asteroids on a collision course with Earth.



1 NASA’s DART spacecraft will leave Earth in 2021, arriving at Didymos in 2022. It will target Didymoon, smashing into it at a speed of 6-7km/s.

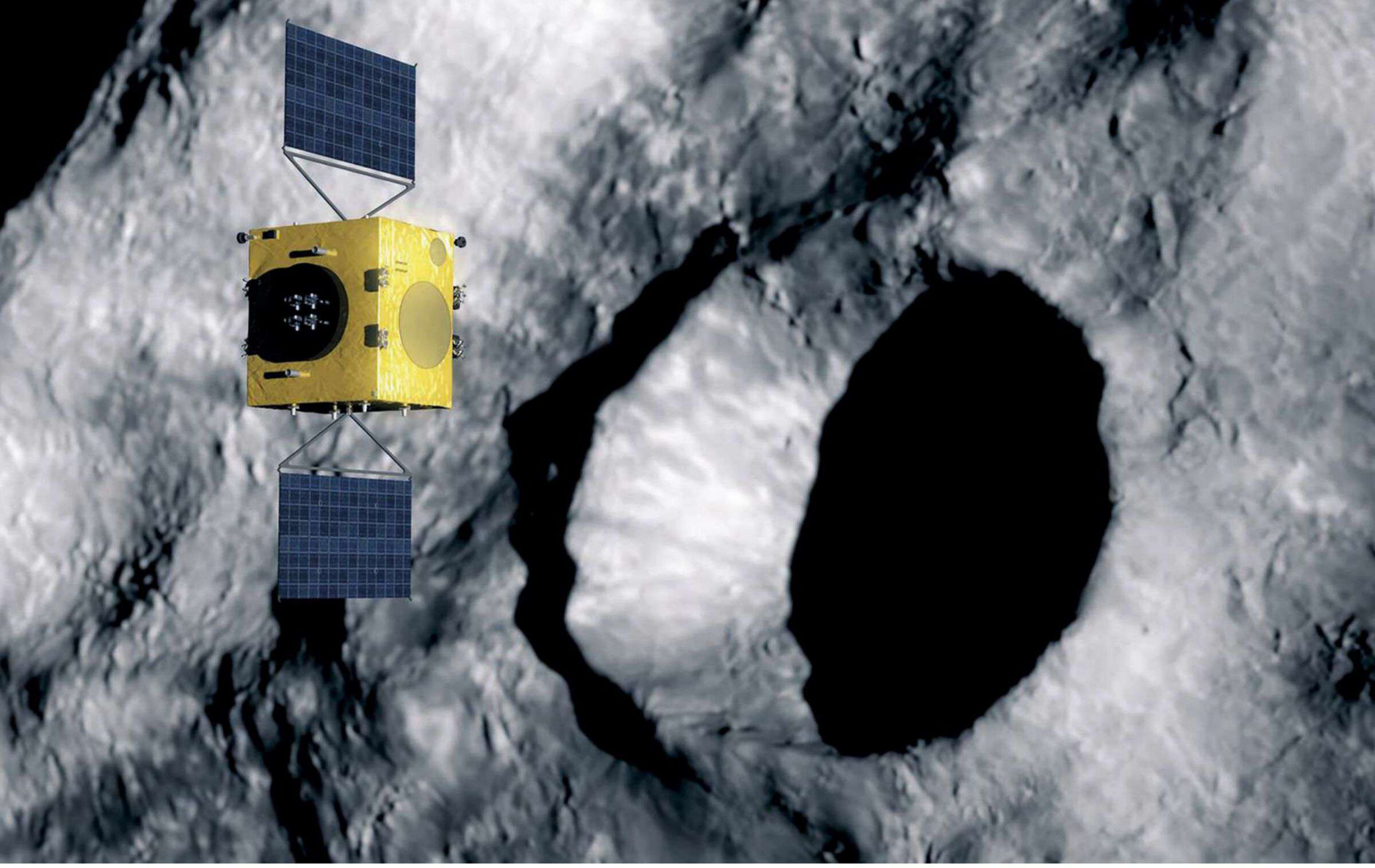
2 DART will be destroyed by the impact, and its orbital energy transferred to Didymoon. It will be like an explosion has gone off, and it will leave behind a big crater.

3 Radar stations and telescopes on Earth will track Didymos and Didymoon to measure the change in velocity caused by the DART impact.

4 ESA’s Hera craft will arrive in 2025. Hera’s job is to measure the impact crater, and investigate Didymoon’s composition and characteristics.

5 Hera will launch two CubeSats, which will land on Didymoon to further study its composition.

“Unlike other natural disasters, asteroid and comet impacts are things that we can actually do something about”



ABOVE Hera will investigate the impact crater caused by DART, assisted by a pair of CubeSat mini satellites

BELOW RIGHT Hera is due to set out from Earth in 2025, but only if funding can be secured

we can't prevent those disasters from happening. Planetary defence against asteroids is different because we *can* do something. "We can cause an impact not to happen," Rivkin says, "We have the technology to do this, and we now want to test it."

DART will close in on Didymoon at a speed of between six and seven kilometres per second, and will hit the space rock when it is roughly 11 million kilometres away from Earth. If the team pulls it off, it will be a staggering achievement in astronautics.

NASA does have some prior experience in this. In 2005, they smashed a spacecraft into comet Tempel 1. Known as the Deep Impact mission, it was a tactic designed to reveal the interior of the comet rather than try to deflect it, but it did give them valuable insight into such space targeting.

In the intervening years, computers and software have also come on apace. To zero in on Didymoon, DART will use software similar to that used at observatories to keep their telescopes pointing at the right target. After the impact, DART will be completely destroyed. "We expect to make a crater 10 to 15 metres across," says Rivkin.

AFTER THE IMPACT

Once DART has carried out its mission, telescopes on Earth will begin tracking Didymos to see if Didymoon has been deflected. Then, in 2025, Hera is scheduled to arrive to begin its work. The European component of the mission will first look at the size and shape of the impact crater made by DART. This will give us the first information about the composition of Didymoon, because different materials will react in different ways to the collision. Hera will also carry a suite of instruments to perform other analyses, allowing it to deduce the asteroid's mass, density and thermal properties. Only by gaining this information can we accurately translate the DART mission's achievements into what we should do if we see another asteroid heading for us in the future. "These properties will help us to simulate deflection impacts more accurately," says Carnelli. He imagines a future time in

"The mission will be a precise deflection test that can be applied to any incoming object in the same size range"

NASA/JOHNS HOPKINS, SCIENCE PHOTO LIBRARY, NASA GSFC X2, GETTY IMAGES, ESA

A PLANET IN PERIL

Asteroids aren't the only space-based hazards that could put our lives in jeopardy...

SPACE DEBRIS

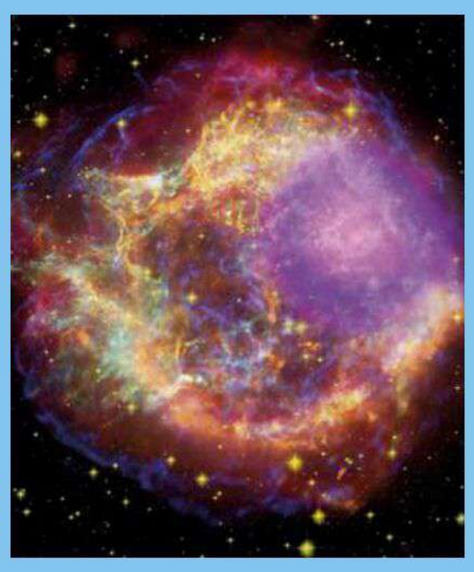
Although unlikely to cause a widespread threat to life on Earth, space debris is a huge concern. It poses a serious risk to orbiting satellites, and because we rely on those satellites for so many things related to communication and navigation, it threatens our way of life.

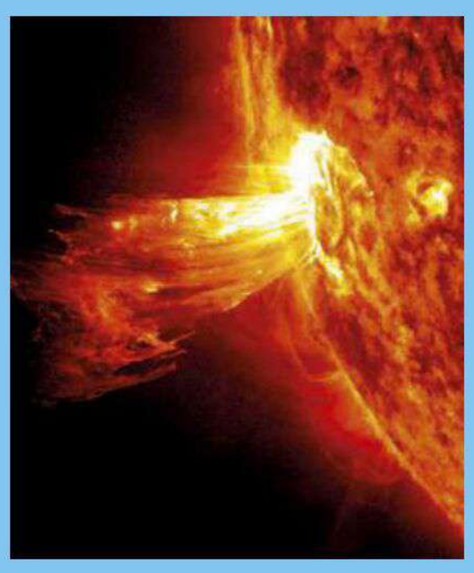
DANGER FACTOR: HIGH

SUPERNOVAE

Exploding stars pose a danger to life because of the torrent of high-energy radiation they would release. To be a risk to us, however, there would need to be a red supergiant star within 50 light-years of Earth. Luckily, no such stars are anywhere near that close.

DANGER FACTOR: NEGLIGIBLE





SOLAR STORMS

Giant releases of magnetic energy on the Sun can propel vast clouds of electrified gas towards us on Earth. These can seriously damage our technology such as satellites and power grids. A large solar storm could cause major disruption through sustained power blackouts and communications outages.

DANGER FACTOR: MODERATE TO HIGH

EVIL ALIENS

We've all seen the films where marauding aliens come to Earth and wreak havoc. In real life, however, astronomers see no evidence for alien technology, which would naturally give off some kind of detectable emission because... physics. So perhaps evil aliens simply don't exist.

DANGER FACTOR: LOW (PROBABLY?)

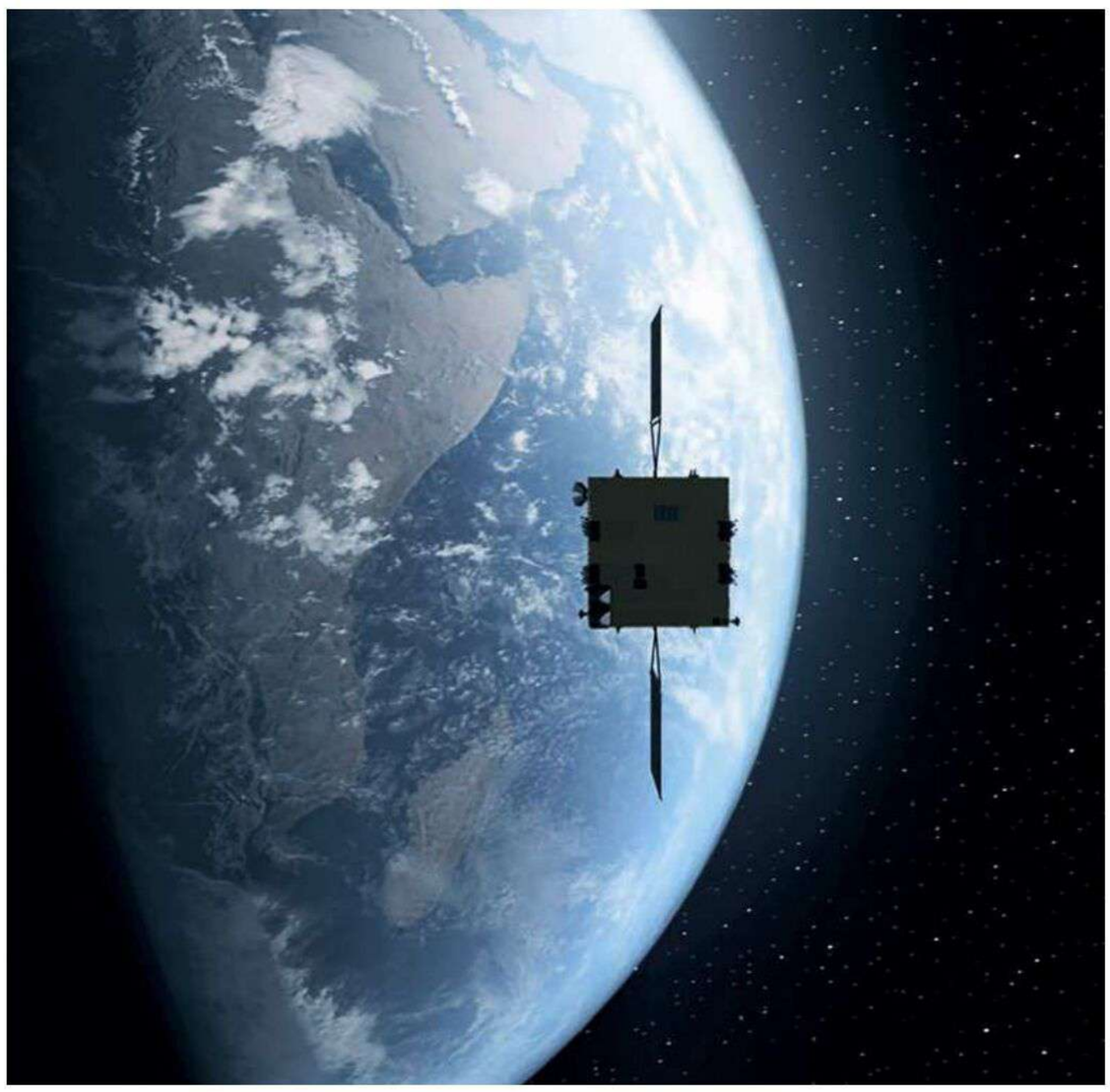
which a hazardous asteroid is spotted coming our way. It can be immediately studied to learn its properties and these numbers can be compared to those of Didymoon. "You put these numbers into the computer and it tells you exactly how hard to hit it to deflect it," says Carnelli.

In other words, Hera completes DART by making the mission a precise deflection test that can be widely applied to any incoming object we detect in this size range. But there is a big hurdle for the mission to cross: funding.

NASA's DART is fully funded. It's being built and will launch next year. Hera needs €140m (£128m approx) from European science ministers this November to be built, and then an additional €160m (£146m approx) in three years' time to be launched and operated. The funding is not guaranteed. A previous version of the mission was rejected in 2016.

For Carnelli, who has been studying asteroid deflection tests at ESA since the early 2000s, this is something of a do-or-die moment. "In 2003-4, asteroid deflection was still quite fictional in terms of asteroid deflection techniques," he says. "I still remember when people were proposing to paint asteroids, or attach them to solar sails, or to anchor some ion propulsion systems. All of this has disappeared. There is a very well-established planetary defence community now. And as a community, we know what we want. We just need to get it done."

Because in real life, we won't have Bruce Willis to save us. **SF**



by **DR STUART CLARK** *(@DrStuClark)*

Stuart is an astronomer and science writer. His latest book is The Search For Earth's Twin *(£12.99, Quercus).*

ALL YOUR QUESTIONS ANSWERED

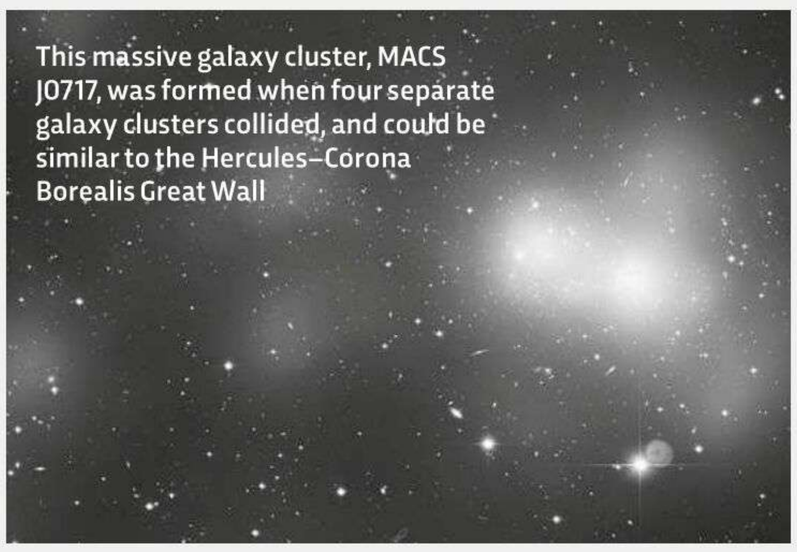
WHAT DOES BIODEGRADABLE PLASTIC DEGRADE INTO?

Biodegradable plastics contain chemical additives that encourage microorganisms to feed on the plastic, using their enzymes to break the plastic's molecular bonds. These additives work in two main ways: either by attracting microbes to the plastic directly or by speeding up the plastic's natural weathering process, which gives a larger, more ragged surface area for the microbes to work on. Once the microbes have done their work, all that's left behind is water, carbon dioxide, and methane. The reality is, however, a little more complex. Many biodegradable plastics need particular conditions in order to biodegrade. This typically involves temperatures of over 50°C and the right combination of moisture, air and microbes – meaning that these plastics won't break down if left in the ocean or on domestic compost heaps. Meanwhile, some plastics labelled as biodegradable aren't truly biodegradable but are merely designed to disintegrate into fragments when exposed to air. These plastics never decompose entirely, but leave behind tiny pieces known as microplastics.

WHATEVER HAPPENED TO IRRADIATED FOOD?

Food waste is a huge problem. In the UK alone, it's estimated we bin over 10 million tonnes of food every year, worth £20bn. Of this, around 20 per cent is due to spoilage from bacterial action. An effective way of reducing spoilage exists, but it's never caught on: exposing food to radiation.

Over 100 years ago, researchers found that X-rays kill off bacteria, and by the late 1950s the first commercial food irradiation plant was operating. Today, the treatment of many types of food using gamma radiation is approved in over 60 countries. Yet despite its ability to cut both food waste and food poisoning, it's never gone mainstream. That's largely because of consumer resistance. Despite hundreds of scientific studies showing it doesn't make food radioactive or impact quality, most people simply won't touch it.



This massive galaxy cluster, MACS J0717, was formed when four separate galaxy clusters collided, and could be similar to the Hercules–Corona Borealis Great Wall

WHAT IS THE LARGEST KNOWN CELESTIAL BODY?

The largest known 'object' is the Hercules-Corona Borealis Great Wall. This 'galactic filament' is a vast cluster of gravity-bound galaxies, approximately 10 billion light-years across! However, a celestial body normally implies a tightly-bound object like a star or a galaxy. The largest known elliptical galaxy is thought to be IC 1101 (with a diameter of four million light-years), and the largest known spiral galaxy is Malin 1 (with a diameter of 650,000 light-years). The largest star is thought to be red hypergiant UY Scuti, in the constellation Scutum, with an estimated radius of over a billion kilometres – 1,700 times that of the Sun.

ALAMY X 3. GETTY IMAGES, NASA, ESA, HARALD EBELING (UNIVERSITY OF HAWAII AT MANOA) & JEAN-PAUL KNEIB (LAM)

WHY AREN'T LARGE LEGO BRICKS USED TO BUILD FULL-SIZE BUILDINGS?

The plastic used in Lego – a polymer called 'acrylonitrile butadiene styrene' (ABS) – is surprisingly strong. In fact, it's able to withstand compression better than concrete. Researchers have found an ordinary Lego brick can support the weight of 375,000 other bricks. Theoretically, that equates to a tower almost 3.5km high! But Lego is too expensive to be used as a building material. There are, however, Lego-style construction techniques that use other materials. 'Insulated concrete formwork' (ICF) uses hollow polystyrene blocks assembled into walls and pumped full of concrete. The polystyrene acts as a mould, providing insulation. In developing countries, interlocking blocks of compressed earth mixed with a little cement are a cheap alternative.

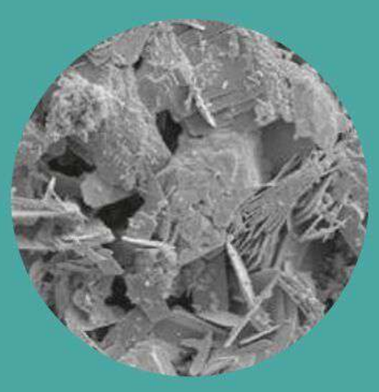
WHAT WOULD HAPPEN IF A PERSON JUST ATE MEAT AND NOTHING ELSE?

Not much – at least in the short term. In a 1928 study, two 'normal' men ate only meat for one year, under the supervision of medical researchers in New York. At the end of the year the men showed "no specific physical changes in any system of the body". Today, fans of a 'carnivore diet' claim it brings weight loss and improves digestive health. But with so much evidence of anti-cancer effects found in plant-based nutrition, the jury is out on whether a meat-only diet is actually healthy in the long term.

WHAT CONNECTS MOUNT VESUVIUS AND CARROTS?

1. Mount Vesuvius, in southern Italy, is the most active volcano in mainland Europe. It has erupted 12 times in the last 200 years, most recently in 1944.

2. Ash from Vesuvius was used in Ancient Rome to make incredibly strong concrete. Concrete piers from Roman harbours, dating back 2,000 years, are still standing, while modern marine concrete can corrode within decades.



3. The strength of Roman concrete comes from aluminium and silica minerals in the ash that crystallise as seawater seeps into microscopic cracks. This helps bind the concrete and prevent larger cracks forming.

4. Nanoparticles of cellulose, taken from root vegetables like carrots, can perform even better. Lancaster University researchers found that carrot-reinforced concrete was more than twice as strong as standard concrete.

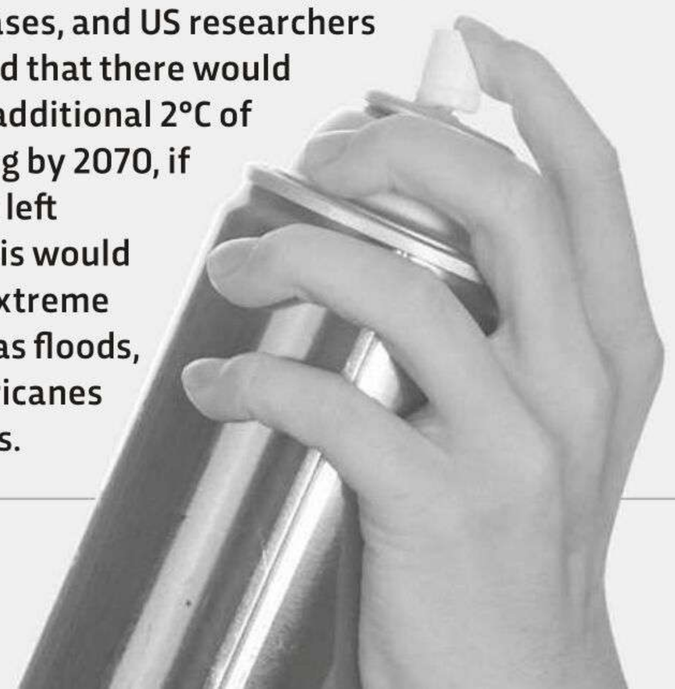
COULD WE LIVE ON AIRSHIPS IN THE ATMOSPHERE OF VENUS?

Although the surface environment of Venus is extremely hostile, there is a region between about 50km and 60km above the surface where atmospheric pressure and temperature are similar to Earth's. In fact, this region may well be the most 'Earth-like' environment in the Solar System. This has inspired the idea of vast floating cities occupying the Venusian atmosphere, without the potentially more difficult and costly process of 'terraforming' the planet below for human habitation. However, space agencies have so far been primarily focused on the possibility of colonising Mars. This is partly because Mars already receives much more attention as a destination for unmanned exploration, and because living in floating cities may be perceived as inherently more dangerous, and also because humans are used to living on terra firma. So it looks like a life amid the clouds will be consigned to sci-fi for now.

WHAT WOULD HAVE HAPPENED IF WE'D CARRIED ON USING CFCs?

In humans, heightened exposure to UVB radiation would have triggered a surge of skin cancer and cataracts. According to one estimate, there would have been an extra two million cases of skin cancer by 2030. By 2065, UV radiation would be three times its current strength, making any Sun exposure deadly.

Overexposure to UVB radiation stunts the growth of many plants, and the resulting decline in agricultural productivity could have triggered food shortages. The radiation also harms phytoplankton – tiny organisms that form the basis of marine food webs – with untold consequences for wider ecosystems. Chlorofluorocarbons (CFCs) are powerful greenhouse gases, and US researchers have calculated that there would have been an additional 2°C of global warming by 2070, if CFCs had been left unchecked. This would have fuelled extreme weather such as floods, droughts, hurricanes and heatwaves.



COULD A pH GREATER THAN 14 EXIST?

The pH scale typically stretches from zero to 14, passing through a neutral pH7 (freshly distilled water). Strong acids have a low pH, while alkaline chemicals, such as bleach, have a high pH. Invented in 1909 by Danish biochemist Søren Sørensen, it describes how many hydrogen ions (protons) are in a solution: the higher the pH, the lower the concentration, and vice versa. But the limits are not fixed, so it *is* possible to go above 14 or below zero. For example, concentrated hydrochloric acid can have a pH of -1, while sodium hydroxide solution can have a pH as high as 15.

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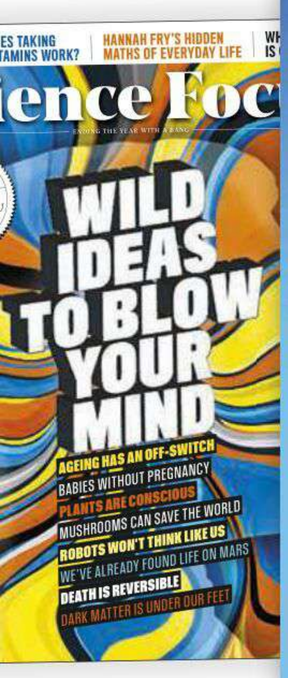

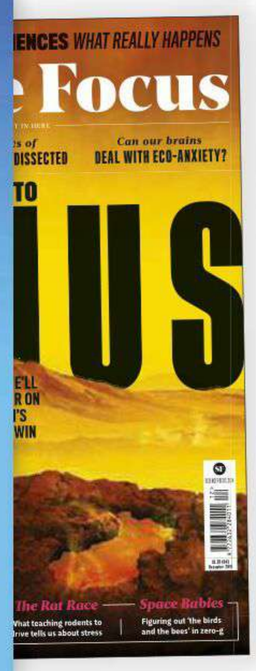

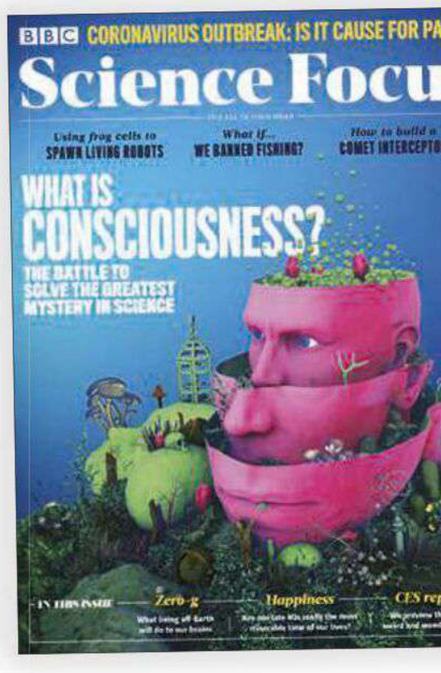

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